(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
11 January 2001 (11.01.2001)

PCT

(10) International Publication Number
WO 01/02568 A2

(51) International Patent Classification[7]: C12N 15/12, 15/55, 15/54, 15/61, C07K 14/47, C12N 9/64, 9/12, 9/90, C12Q 1/68, C12N 15/11, C07K 16/18, 16/40, G01N 33/566, A61K 38/00

(21) International Application Number: PCT/US00/18374

(22) International Filing Date: 30 June 2000 (30.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/142,310	2 July 1999 (02.07.1999)	US
60/142,311	2 July 1999 (02.07.1999)	US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/02568 A2

(54) Title: NOVEL HUMAN GENES AND GENE EXPRESSION PRODUCTS

(57) Abstract: The invention provides novel polynucleotides. The invention further provides novel members of protein families, and polynucleotides that are differentially expressed in cancer cells relative to normal cells, and in metastatic cancer cells relative to normal cells or non-metastatic cancer cells.

NOVEL HUMAN GENES AND GENE EXPRESSION PRODUCTS

FIELD OF THE INVENTION

The present invention relates to novel polynucleotides of human origin and the encoded gene products.

BACKGROUND OF THE INVENTION

Identification of novel polynucleotides, particularly those that encode an expressed gene product, is important in the advancement of drug discovery, diagnostic technologies, and the understanding of the progression and nature of complex diseases such as cancer. Identification of genes expressed in different cell types isolated from sources that differ in disease state or stage, developmental stage, exposure to various environmental factors, the tissue of origin, the species from which the tissue was isolated, and the like is key to identifying the genetic factors that are responsible for the phenotypes associated with these various differences.

This invention provides novel human polynucleotides, the polypeptides encoded by these polynucleotides, and the genes and proteins corresponding to these novel polynucleotides.

SUMMARY OF THE INVENTION

This invention relates to novel human polynucleotides and variants thereof, their encoded polypeptides and variants thereof, to genes corresponding to these polynucleotides and to proteins expressed by the genes. The invention also relates to diagnostics and therapeutics comprising such novel human polynucleotides, their corresponding genes or gene products, including probes, antisense nucleotides, and antibodies. The polynucleotides of the invention correspond to a polynucleotide comprising the sequence information of at least one of SEQ ID NOs: 1-3351.

Various aspects and embodiments of the invention will be readily apparent to the ordinarily skilled artisan upon reading the description provided herein.

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to polynucleotides comprising the disclosed nucleotide sequences, to full length cDNA, mRNA genomic sequences, and genes

corresponding to these sequences and degenerate variants thereof, and to polypeptides encoded by the polynucleotides of the invention and polypeptide variants.

Polypeptide variants differ from wild type protein in having one or more amino acid substitutions that either enhance, add, or diminish a biological activity of the wild type protein.

Six of the polypeptides disclosed herein encode new members of the MKK kinase family; the coding region is found within the nucleotide region in parentheses: SEQ ID NO:29 (nucleotides 295-421); SEQ ID NO:31 (298-397); SEQ ID NO:196 (37-322); SEQ ID NO:3175 (nucleotides 14-164); SEQ ID NO:3190 (229-390); and SEQ ID NO:3281 (15-182). Twenty-four of the polypeptides encode new members of the family of transcription factor proteins having a basic region plus leucine zipper: SEQ ID NO:410 (42-191); SEQ ID NO:552 (116-288); SEQ ID NO:768 (116-288); SEQ ID NO:822 (108-262); SEQ ID NO:836 (158-353); SEQ ID NO:1288 (73-234); SEQ ID NO:1365 (69-257); SEQ ID NO:1540 (289-471); SEQ ID NO:1549 (200-391); SEQ ID NO:1556 (163-354); SEQ ID NO:1557 (207-398); SEQ ID NO:1563 (107-298); SEQ ID NO:1622 (180-365); SEQ ID NO:1630 (100-291); SEQ ID NO:1704 (184-372); SEQ ID NO:1808 (36-161); SEQ ID NO:1454 (49-209); SEQ ID NO:2363 (48-211); SEQ ID NO:2424 (43-194); SEQ ID NO:3147 (190-369); SEQ ID NO:3152 (129-320); SEQ ID NO:3158 (167-334); and SEQ ID NO:3208 (34-256).

SEQ ID NOs:186 (175-395); 2591 (60-165); 3307 (43-321); and 3339 (94-342) encode polypeptides having an SH2 domain, and SEQ ID NOs:234 (23-121), 1832 (18-173), and 1835 (57-206) encode polypeptides having an SH3 domain. Nine polypeptides encode new members of the family of proteins having Ank repeat regions: SEQ ID NO:187 (358-432); SEQ ID NO:1268 (238-315); SEQ ID NO:1804 (301-378); SEQ ID NO:1819 (278-355); SEQ ID NO:1839 (224-307); SEQ ID NO:1830 (184-267); SEQ ID NO:2562 (18-101); SEQ ID NO:3015 (131-214); and SEQ ID NO:3267 (97-180).

The following eleven polynucleotides encode polypeptides having a C2H2 type zinc finger: SEQ ID NOs:308 (110-172); 807 (339-392); 1324 (294-356); 1503 (154-216); 1527 (156-212); 1674 (196-258); 1779 (64-126); 1801 (295-351); 3081 (190-252); 3193 (293-355); and 3306 (161-223). Eight polynucleotides encode polypeptides of the family of ATPases: SEQ ID NOs:431 (71-428); 639 (157-561); 2135 (2-401); 2684 (9-461); 2859 (100-320); 3178 (45-386); 3197 (281-343) and 3266 (8-139). Polypeptides having a fibronectin type III domain are encoded by SEQ ID NO:746 (209-427) and 1192 (186-416). Polypeptides having an EF-hand domain are encoded by SEQ ID NO:820 (341-

406); 1755 (281-367) and 3285(16-102). Six polypeptides of the protein kinase family are encoded by SEQ ID NOs:1157 (41-444); 1478 (54-437), 1496 (241-520); 2286 (12-182); 2969 (5-387); and 3190 (118-390).

LIM domain-containing polypeptides are encoded by SEQ ID NO:1269 (79-240); 1309 (248-404); 1360 (222-377); and 1386 (243-398). Two polypeptides of the family having a C2 domain (protein kinase C-like) are encoded by SEQ ID NO:1325 (1-234) and 2282(183-353). Polypeptides having a WD domain, G-beta repeat motif are encoded by SEQ ID NOs:1336 (66-164); 1380 (42-140); 1711 (263-361); 1762 (236-334); 1909 (160-258); 2218 (127-225); 3047 (191-292); 3108 (275-367) and 3292 (208-300).

SEQ ID NO:1410 (222-350) encodes a member of the trypsin family. SEQ ID NOs:1417 (8-354); 2281 (20-387) and 2310 (20-371) encode members of the protein tyrosine phosphatase family. SEQ ID NOs:1464 (4-180) and 1514 (2-252) encode members of the family having an RNA recognition motif (also known as RRM, RBD, or RNP domain). SEQ ID NOs:1496 (241-520) and 3297(7-153) encode helicases having a conserved C-terminal domain. SEQ ID NO:1538 (9-635) encodes a member of the wnt family of developmental signaling proteins.

Three polynucleotides encode polypeptides having a homeobox domain: SEQ ID NOs:1676 (9-86); 1820 (123-299); and 1821 (127-303). A novel thioredoxin is encoded by SEQ ID NO:1677 (316-369). Two novel members of the ras family are encoded by SEQ ID NO:1688(109-410) and 3258(138-394). A novel polypeptide having a phosphatidylinositol-specific phospholipase C Y-domain is encoded by SEQ ID NO:1707 (92-439). A novel serine carboxypeptidase is encoded by SEQ ID NO:1744 (238-433). A novel polypeptide having N-terminal homology in the Ets domain is encoded by SEQ ID NO:1811 (184-315). A novel polypeptide having a bromodomain is encoded by SEQ ID NO:1814 (127-294). A novel polypeptide having a double-stranded RNA binding motif is encoded by SEQ ID NO:1818 (9-146). A novel polypeptide having a G-protein alpha subunit is encoded by SEQ ID NO:1846 (12-398).

SEQ ID NOs:1911 (35-151) and 1980 (60-197) encode polypeptides having a C3HC4 type zinc finger domain (RING finger). SEQ ID NO:2065 (253-306) encodes a polypeptide having a CCHC zinc finger domain. SEQ ID NO:2216 (90-179) encodes a polypeptide having a WW/rsp5/WWP domain. SEQ ID NO:2428 (25-350) encodes a polypeptide member of the dual specificity phosphatase family, having a catalytic domain.

SEQ ID NOs:2577 (0-311); 3183 (14-215); and 3195 (0-215) encode members of the 4 transmembrane segment integral membrane protein family. SEQ ID

NOs:2826 (116-400) and 2871 (198-392) encode polypeptides of the DEAD and DEAH box helicase family. SEQ ID NO:2944 (18-281) encodes a polypeptide having a calpain large subunit, domain III.

SEQ ID NO:3274 (11-187) encodes a eukaryotic transcription factor with a fork head domain. SEQ ID NO:3345 (65-271) encodes a polypeptide having a PDZ domain, and SEQ ID NO:3351 (124-270) encodes a polypeptide in the family of phorbol esters/glycerol binding proteins.

Described below are polynucleotide compositions encompassed by the invention, methods for obtaining cDNA or genomic DNA encoding a full-length gene product, expression of these polynucleotides and genes, identification of structural motifs of the polynucleotides and genes, identification of the function of a gene product encoded by a gene corresponding to a polynucleotide of the invention, use of the provided polynucleotides as probes and in mapping and in tissue profiling, use of the corresponding polypeptides and other gene products to raise antibodies, and use of the polynucleotides and their encoded gene products for therapeutic and diagnostic purposes.

Polynucleotide Compositions

The scope of the invention with respect to polynucleotide compositions includes, but is not necessarily limited to, polynucleotides having a sequence set forth in any one of SEQ ID NOs:1-3351; polynucleotides obtained from the biological materials described herein or other biological sources (particularly human sources) by hybridization under stringent conditions (particularly conditions of high stringency); genes corresponding to the provided polynucleotides; variants of the provided polynucleotides and their corresponding genes, particularly those variants that retain a biological activity of the encoded gene product (*e.g.*, a biological activity ascribed to a gene product corresponding to the provided polynucleotides as a result of the assignment of the gene product to a protein family(ies) and/or identification of a functional domain present in the gene product). Other nucleic acid compositions contemplated by and within the scope of the present invention will be readily apparent to one of ordinary skill in the art when provided with the disclosure here. "Polynucleotide" and "nucleic acid" as used herein with reference to nucleic acids of the composition is not intended to be limiting as to the length or structure of the nucleic acid unless specifically indicated.

The invention features polynucleotides that are expressed in human tissue, specifically human colon, breast, and/or lung tissue. Novel nucleic acid

compositions of the invention comprise a sequence set forth in any one of SEQ ID NOs:1-3351 or an identifying sequence thereof. An "identifying sequence" is a contiguous sequence of residues at least about 10 nt to about 20 nt in length, usually at least about 50 nt to about 100 nt in length, that uniquely identifies a polynucleotide sequence, *e.g.*, exhibits less than 90%, usually less than about 80% to about 85% sequence identity to any contiguous nucleotide sequence of more than about 20 nt. Thus, the subject novel nucleic acid compositions include full length cDNAs or mRNAs that encompass an identifying sequence of contiguous nucleotides from any one of SEQ ID NOs:1-3351.

The polynucleotides of the invention also include polynucleotides having sequence similarity or sequence identity. Nucleic acids having sequence similarity are detected by hybridization under low stringency conditions, for example, at 50°C and 10XSSC (0.9 M saline/0.09 M sodium citrate) and remain bound when subjected to washing at 55°C in 1XSSC. Sequence identity can be determined by hybridization under stringent conditions, for example, at 50°C or higher and 0.1XSSC (9 mM saline/0.9 mM sodium citrate). Hybridization methods and conditions are well known in the art, see, *e.g.*, U.S. Patent No. 5,707,829. Nucleic acids that are substantially identical to the provided polynucleotide sequences, *e.g.*, allelic variants, genetically altered versions of the gene, *etc.*, bind to the provided polynucleotide sequences (SEQ ID NOs:1-3351) under stringent hybridization conditions. By using probes, particularly labeled probes of DNA sequences, one can isolate homologous or related genes. The source of homologous genes can be any species, *e.g.*, primate species, particularly human; rodents, such as rats and mice; canines, felines, bovines, ovines, equines, yeast, nematodes, *etc.*

Preferably, hybridization is performed using at least 15 contiguous nucleotides (nt) of at least one of SEQ ID NOs:1-3351. That is, when at least 15 contiguous nt of one of the disclosed SEQ ID NOs. is used as a probe, the probe will preferentially hybridize with a nucleic acid comprising the complementary sequence, allowing the identification and retrieval of the nucleic acids that uniquely hybridize to the selected probe. Probes from more than one SEQ ID NO. can hybridize with the same nucleic acid if the cDNA from which they were derived corresponds to one mRNA. Probes of more than 15 nt can be used, *e.g.*, probes of from about 18 nt to about 100 nt, but 15 nt represents sufficient sequence for unique identification.

The polynucleotides of the invention also include naturally occurring variants of the nucleotide sequences (*e.g.*, degenerate variants, allelic variants).

Variants of the polynucleotides of the invention are identified by hybridization of putative variants with nucleotide sequences disclosed herein, preferably by hybridization under stringent conditions. For example, by using appropriate wash conditions, variants of the polynucleotides of the invention can be identified where the allelic variant exhibits at most about 25-30% base pair (bp) mismatches relative to the selected polynucleotide probe. In general, allelic variants contain 15-25% bp mismatches, and can contain as little as even 5-15%, or 2-5%, or 1-2% bp mismatches, as well as a single bp mismatch.

The invention also encompasses homologs corresponding to the polynucleotides of SEQ ID NOs:1-3351, where the source of homologous genes can be any mammalian species, *e.g.*, primate species, particularly human; rodents, such as rats; canines, felines, bovines, ovines, equines, yeast, nematodes, *etc.* Between mammalian species, *e.g.*, human and mouse, homologs generally have substantial sequence similarity, *e.g.*, at least 75% sequence identity, usually at least 90%, more usually at least 95% between nucleotide sequences. Sequence similarity is calculated based on a reference sequence, which may be a subset of a larger sequence, such as a conserved motif, coding region, flanking region, *etc.* A reference sequence will usually be at least about 18 contiguous nt long, more usually at least about 30 nt long, and may extend to the complete sequence that is being compared. Algorithms for sequence analysis are known in the art, such as BLAST, described in Altschul et al., *J. Mol. Biol.* (1990) *215*:403-10.

In general, variants of the invention have a sequence identity greater than at least about 65%, preferably at least about 75%, more preferably at least about 85%, and can be greater than at least about 90%, 91%, 92%, 93%, 94%, 95%, or 96%, most preferably 97%, 98% or 99%. For the purposes of this invention, a preferred method of calculating percent identity is the Smith-Waterman algorithm, using the following. Global DNA sequence identity must be greater than 65% as determined by the Smith-Waterman homology search algorithm as implemented in MPSRCH program (Oxford Molecular) using an affine gap search with the following search parameters: gap open penalty, 12; and gap extension penalty, 1.

The subject nucleic acids can be cDNAs or genomic DNAs, as well as fragments thereof, particularly fragments that encode a biologically active gene product and/or are useful in the methods disclosed herein (*e.g.*, in diagnosis, as a unique identifier of a differentially expressed gene of interest, *etc.*). The term "cDNA" as used herein is intended to include all nucleic acids that share the arrangement of sequence

elements found in native mature mRNA species, where sequence elements are exons and 3' and 5' non-coding regions. Normally mRNA species have contiguous exons, with the intervening introns, when present, being removed by nuclear RNA splicing, to create a continuous open reading frame encoding a polypeptide of the invention.

A genomic sequence of interest comprises the nucleic acid present between the initiation codon and the stop codon, as defined in the listed sequences, including all of the introns that are normally present in a native chromosome. It can further include the 3' and 5' untranslated regions found in the mature mRNA. It can further include specific transcriptional and translational regulatory sequences, such as promoters, enhancers, *etc.*, including about 1 kb, but possibly more, of flanking genomic DNA at either the 5' and 3' end of the transcribed region. The genomic DNA can be isolated as a fragment of 100 kbp or smaller; and substantially free of flanking chromosomal sequence. The genomic DNA flanking the coding region, either 3' and 5', or internal regulatory sequences as sometimes found in introns, contains sequences required for proper tissue, stage-specific, or disease-state specific expression.

The nucleic acid compositions of the subject invention can encode all or a part of the subject polypeptides. Double or single stranded fragments can be obtained from the DNA sequence by chemically synthesizing oligonucleotides in accordance with conventional methods, by restriction enzyme digestion, by PCR amplification, *etc.* Isolated polynucleotides and polynucleotide fragments of the invention comprise at least about 10, about 15, about 20, about 35, about 50, about 100, about 150 to about 200, about 250 to about 300, or about 350 contiguous nt selected from the polynucleotide sequences as shown in SEQ ID NOs:1-3351. The fragments also include those of lengths intermediate to the specifically mentioned lengths, such as 35, 36, 37, 38, 39, etc.; 150, 151, 152, 153, 154, etc. For the most part, fragments will be of at least 15 nt, usually at least 18 nt or 25 nt, and up to at least about 50 contiguous nt in length or more. In a preferred embodiment, the polynucleotide molecules comprise a contiguous sequence of at least 12 nt selected from the group consisting of the polynucleotides shown in SEQ ID NOs:1-3351.

Probes specific to the polynucleotides of the invention can be generated using the polynucleotide sequences disclosed in SEQ ID NOs:1-3351. The probes are preferably at least about a 12, 15, 16, 18, 20, 22, 24, or 25 nt fragment of a corresponding contiguous sequence of SEQ ID NOs:1-3351, and can be less than 2, 1, 0.5, 0.1, or 0.05 kb in length. The probes can be synthesized chemically or can be generated from longer polynucleotides using restriction enzymes. The probes can be

labeled, for example, with a radioactive, biotinylated, or fluorescent tag. Preferably, probes are designed based upon an identifying sequence of a polynucleotide of one of SEQ ID NOs:1-3351. More preferably, probes are designed based on a contiguous sequence of one of the subject polynucleotides that remain unmasked following application of a masking program for masking low complexity (*e.g.*, XBLAST) to the sequence., *i.e.*, one would select an unmasked region, as indicated by the polynucleotides outside the poly-n stretches of the masked sequence produced by the masking program.

The polynucleotides of the subject invention are isolated and obtained in substantial purity, generally as other than an intact chromosome. Usually, the polynucleotides, either as DNA or RNA, will be obtained substantially free of other naturally-occurring nucleic acid sequences, generally being at least about 50%, usually at least about 90% pure and are typically "recombinant", *e.g.*, flanked by one or more nucleotides with which it is not normally associated on a naturally occurring chromosome.

The polynucleotides of the invention can be provided as a linear molecule or within a circular molecule, and can be provided within autonomously replicating molecules (vectors) or within molecules without replication sequences. Expression of the polynucleotides can be regulated by their own or by other regulatory sequences known in the art. The polynucleotides of the invention can be introduced into suitable host cells using a variety of techniques available in the art, such as transferrin polycation-mediated DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated DNA transfer, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, gene gun, calcium phosphate-mediated transfection, and the like.

The subject nucleic acid compositions can be used to, for example, produce polypeptides, as probes for the detection of mRNA of the invention in biological samples (*e.g.*, extracts of human cells) to generate additional copies of the polynucleotides, to generate ribozymes or antisense oligonucleotides, and as single stranded DNA probes or as triple-strand forming oligonucleotides. The probes described herein can be used to, for example, determine the presence or absence of the polynucleotide sequences as shown in SEQ ID NOs:1-3351 or variants thereof in a sample. These and other uses are described in more detail below.

Use of Polynucleotides to Obtain Full-Length cDNA, Gene, and Promoter Region

Full-length cDNA molecules comprising the disclosed polynucleotides are obtained as follows. A polynucleotide having a sequence of one of SEQ ID NOs:1-3351, or a portion thereof comprising at least 12, 15, 18, or 20 nt, is used as a hybridization probe to detect hybridizing members of a cDNA library using probe design methods, cloning methods, and clone selection techniques such as those described in U.S. Patent No. 5,654,173. Libraries of cDNA are made from selected tissues, such as normal or tumor tissue, or from tissues of a mammal treated with, for example, a pharmaceutical agent. Preferably, the tissue is the same as the tissue from which the polynucleotides of the invention were isolated, as both the polynucleotides described herein and the cDNA represent expressed genes. Most preferably, the cDNA library is made from the biological material described herein in the Examples. The choice of cell type for library construction can be made after the identity of the protein encoded by the gene corresponding to the polynucleotide of the invention is known. This will indicate which tissue and cell types are likely to express the related gene, and thus represent a suitable source for the mRNA for generating the cDNA. As described in the Examples, cDNA of the invention was isolated from specific cell or tissue types, and such cells and tissues are preferable for obtaining related nucleic acids.

Techniques for producing and probing nucleic acid sequence libraries are described, for example, in Sambrook et al., *Molecular Cloning: A Laboratory Manual, 2nd Ed.*, (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY. The cDNA can be prepared by using primers based on sequence from SEQ ID NOs:1-3351. In one embodiment, the cDNA library can be made from only poly-adenylated mRNA. Thus, poly-T primers can be used to prepare cDNA from the mRNA.

Members of the library that are larger than the provided polynucleotides, and preferably that encompass the complete coding sequence of the native message, are obtained. In order to confirm that the entire cDNA has been obtained, RNA protection experiments are performed as follows. Hybridization of a full-length cDNA to an mRNA will protect the RNA from RNase degradation. If the cDNA is not full length, then the portions of the mRNA that are not hybridized will be subject to RNase degradation. This is assayed, as is known in the art, by changes in electrophoretic mobility on polyacrylamide gels, or by detection of released monoribonucleotides. Sambrook et al., *Molecular Cloning: A Laboratory Manual, 2nd Ed.*, (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY. In order to obtain additional sequences

5' to the end of a partial cDNA, 5' RACE (*PCR Protocols: A Guide to Methods and Applications*, (1990) Academic Press, Inc.) can be performed.

Genomic DNA is isolated using the provided polynucleotides in a manner similar to the isolation of full-length cDNAs. Briefly, the provided polynucleotides, or portions thereof, are used as probes to libraries of genomic DNA. Preferably, the library is obtained from the cell type that was used to generate the polynucleotides of the invention, but this is not essential. Most preferably, the genomic DNA is obtained from the biological material described herein in the Examples. Such libraries can be in vectors suitable for carrying large segments of a genome, such as P1 or YAC, as described in detail in Sambrook et al., 9.4-9.30. In addition, genomic sequences can be isolated from human BAC libraries, which are commercially available from Research Genetics, Inc., Huntsville, Alabama, USA, for example. In order to obtain additional 5' or 3' sequences, chromosome walking is performed, as described in Sambrook et al., such that adjacent and overlapping fragments of genomic DNA are isolated. These are mapped and pieced together, as is known in the art, using restriction digestion enzymes and DNA ligase.

Using the polynucleotide sequences of the invention, corresponding full-length genes can be isolated using both classical and PCR methods to construct and probe cDNA libraries. Using either method, Northern blots, preferably, are performed on a number of cell types to determine which cell lines express the gene of interest at the highest level. Classical methods of constructing cDNA libraries are taught in Sambrook et al., *supra*. With these methods, cDNA can be produced from mRNA and inserted into viral or expression vectors. Typically, libraries of mRNA comprising poly(A) tails can be produced with poly(T) primers. Similarly, cDNA libraries can be produced using the instant sequences as primers.

PCR methods are used to amplify the members of a cDNA library that comprise the desired insert. In this case, the desired insert will contain sequence from the full length cDNA that corresponds to the instant polynucleotides. Such PCR methods include gene trapping and RACE methods as described in Gruber et al., WO 95/04745 and Gruber et al., U.S. Patent No. 5,500,356. Kits are commercially available to perform gene trapping experiments from, for example, Life Technologies, Gaithersburg, Maryland, USA. In preferred embodiments of RACE, a common primer is designed to anneal to an arbitrary adaptor sequence ligated to cDNA ends (Apte and Siebert, *Biotechniques* (1993) *15*:890-893; Edwards et al., *Nuc. Acids Res.* (1991) *19*:5227-5232). When a single gene-specific RACE primer is paired with the common

primer, preferential amplification of sequences between the single gene specific primer and the common primer occurs. Commercial cDNA pools modified for use in RACE are available.

The promoter region of a gene generally is located 5' to the initiation site for RNA polymerase II. Hundreds of promoter regions contain the "TATA" box, a sequence such as TATTA or TATAA, which is sensitive to mutations. The promoter region can be obtained by performing 5' RACE using a primer from the coding region of the gene. Alternatively, the cDNA can be used as a probe for the genomic sequence, and the region 5' to the coding region is identified by "walking up." If the gene is highly expressed or differentially expressed, the promoter from the gene can be of use in a regulatory construct for a heterologous gene.

Once the full-length cDNA or gene is obtained, DNA encoding variants can be prepared by site-directed mutagenesis, described in detail in Sambrook et al., 15.3-15.63. The choice of codon or nucleotide to be replaced can be based on disclosure herein on optional changes in amino acids to achieve altered protein structure and/or function.

As an alternative method to obtaining DNA or RNA from a biological material, nucleic acid comprising nucleotides having the sequence of one or more polynucleotides of the invention can be synthesized. Thus, the invention encompasses nucleic acid molecules ranging in length from 15 nt (corresponding to at least 15 contiguous nt of one of SEQ ID NOs:1-3351) up to a maximum length suitable for one or more biological manipulations, including replication and expression, of the nucleic acid molecule. The invention includes but is not limited to (a) nucleic acid having the size of a full gene, and comprising at least one of SEQ ID NOs:1-3351; (b) the nucleic acid of (a) also comprising at least one additional polynucleotide or gene, operably linked to permit expression of a fusion protein; (c) an expression vector comprising (a) or (b); (d) a plasmid comprising (a) or (b) ; and (e) a recombinant viral particle comprising (a) or (b). Once provided with the polynucleotides disclosed herein, construction or preparation of (a) - (e) are well within the skill in the art.

The sequence of a nucleic acid comprising at least 15 contiguous nt of at least any one of SEQ ID NOs:1-3351, preferably the entire sequence of at least any one of SEQ ID NOs:1-3351, is not limited and can be any sequence of A, T, G, and/or C (for DNA) and A, U, G, and/or C (for RNA) or modified bases thereof, including inosine and pseudouridine. The choice of sequence will depend on the desired function and can be dictated by coding regions desired, the intron-like regions desired, and the

regulatory regions desired. Where the entire sequence of any one of SEQ ID NOs:1-3351 is within the nucleic acid, the nucleic acid obtained is referred to herein as a polynucleotide comprising the sequence of any one of SEQ ID NOs:1-3351.

Expression of Polypeptide Encoded by Full-Length cDNA or Full-Length Gene

The provided polynucleotides (*e.g.*, a polynucleotide having a sequence of one of SEQ ID NOs:1-3351), the corresponding cDNA, or the full-length gene is used to express a partial or complete gene product. Constructs of polynucleotides having sequences of SEQ ID NOs:1-3351 can be generated synthetically. Alternatively, single-step assembly of a gene and entire plasmid from large numbers of oligodeoxyribonucleotides is described by, *e.g.*, Stemmer et al., *Gene (Amsterdam)* (1995) *164*(*1*):49-53. In this method, assembly PCR (the synthesis of long DNA sequences from large numbers of oligodeoxyribonucleotides (oligos)) is described. The method is derived from DNA shuffling (Stemmer, *Nature* (1994) *370*:389-391), and does not rely on DNA ligase, but instead relies on DNA polymerase to build increasingly longer DNA fragments during the assembly process.

Appropriate polynucleotide constructs are purified using standard recombinant DNA techniques as described in, for example, Sambrook et al., *Molecular Cloning: A Laboratory Manual, 2nd Ed.*, (1989) Cold Spring Harbor Press, Cold Spring Harbor, NY, and under current regulations described in United States Dept. of HHS, National Institute of Health (NIH) Guidelines for Recombinant DNA Research. The gene product encoded by a polynucleotide of the invention is expressed in any expression system, including, for example, bacterial, yeast, insect, amphibian and mammalian systems. Vectors, host cells and methods for obtaining expression in same are well known in the art. Suitable vectors and host cells are described in U.S. Patent No. 5,654,173.

Polynucleotide molecules comprising a polynucleotide sequence provided herein are generally propagated by placing the molecule in a vector. Viral and non-viral vectors are used, including plasmids. The choice of plasmid will depend on the type of cell in which propagation is desired and the purpose of propagation. Certain vectors are useful for amplifying and making large amounts of the desired DNA sequence. Other vectors are suitable for expression in cells in culture. Still other vectors are suitable for transfer and expression in cells in a whole animal or person. The choice of appropriate vector is well within the skill of the art. Many such vectors are

available commercially. Methods for preparation of vectors comprising a desired sequence are well known in the art.

The polynucleotides set forth in SEQ ID NOs:1-3351 or their corresponding full-length polynucleotides are linked to regulatory sequences as appropriate to obtain the desired expression properties. These can include promoters (attached either at the 5' end of the sense strand or at the 3' end of the antisense strand), enhancers, terminators, operators, repressors, and inducers. The promoters can be regulated or constitutive. In some situations it may be desirable to use conditionally active promoters, such as tissue-specific or developmental stage-specific promoters. These are linked to the desired nucleotide sequence using the techniques described above for linkage to vectors. Any techniques known in the art can be used.

When any appropriate host cells or organisms are used to replicate and/or express the polynucleotides or nucleic acids of the invention, the resulting replicated nucleic acid, RNA, expressed protein or polypeptide, is within the scope of the invention as a product of the host cell or organism. The product is recovered by any appropriate means known in the art.

Once the gene corresponding to a selected polynucleotide is identified, its expression can be regulated in the cell to which the gene is native. For example, an endogenous gene of a cell can be regulated by an exogenous regulatory sequence as disclosed in U.S. Patent No. 5,641,670.

Identification of Functional and Structural Motifs of Novel Genes

Translations of the nucleotide sequence of the provided polynucleotides, cDNAs or full genes can be aligned with individual known sequences. Similarity with individual sequences can be used to determine the activity of the polypeptides encoded by the polynucleotides of the invention. Also, sequences exhibiting similarity with more than one individual sequence can exhibit activities that are characteristic of either or both individual sequences.

The full length sequences and fragments of the polynucleotide sequences of the nearest neighbors can be used as probes and primers to identify and isolate the full length sequence corresponding to provided polynucleotides. The nearest neighbors can indicate a tissue or cell type to be used to construct a library for the full-length sequences corresponding to the provided polynucleotides.

Typically, a selected polynucleotide is translated in all six frames to determine the best alignment with the individual sequences. The sequences disclosed

herein in the Sequence Listing are in a 5' to 3' orientation and translation in three frames can be sufficient. These amino acid sequences are referred to, generally, as query sequences, which will be aligned with the individual sequences. Databases with individual sequences are described in "Computer Methods for Macromolecular Sequence Analysis" *Methods in Enzymology* (1996) *266*, Doolittle, Academic Press, Inc., a division of Harcourt Brace & Co., San Diego, California, USA. Databases include Genbank, EMBL, and DNA Database of Japan (DDBJ).

Query and individual sequences can be aligned using the methods and computer programs described above, and include BLAST, available over the world wide web at http://www.ncbi.nlm.nhi.gov/BLAST. Another alignment algorithm is Fasta, available in the Genetics Computing Group (GCG) package, Madison, Wisconsin, USA, a wholly owned subsidiary of Oxford Molecular Group, Inc. Other techniques for alignment are described in Doolittle, *supra*. Preferably, an alignment program that permits gaps in the sequence is utilized to align the sequences. The Smith-Waterman is one type of algorithm that permits gaps in sequence alignments. See *Meth. Mol. Biol.* (1997) *70*: 173-187. Also, the GAP program using the Needleman and Wunsch alignment method can be utilized to align sequences. An alternative search strategy uses MPSRCH software, which runs on a MASPAR computer. MPSRCH uses a Smith-Waterman algorithm to score sequences on a massively parallel computer. This approach improves ability to identify sequences that are distantly related matches, and is especially tolerant of small gaps and nucleotide sequence errors. Amino acid sequences encoded by the provided polynucleotides can be used to search both protein and DNA databases.

High Similarity. In general, in alignment results considered to be of high similarity, the percent of the alignment region length is typically at least about 55% of total length query sequence; more typically, at least about 58%; even more typically; at least about 60% of the total residue length of the query sequence. Usually, percent length of the alignment region can be as much as about 62%; more usually, as much as about 64%; even more usually, as much as about 66%. Further, for high similarity, the region of alignment, typically, exhibits at least about 75% of sequence identity; more typically, at least about 78%; even more typically; at least about 80% sequence identity. Usually, percent sequence identity can be as much as about 82%; more usually, as much as about 84%; even more usually, as much as about 86%.

The p value is used in conjunction with these methods. If high similarity is found, the query sequence is considered to have high similarity with a profile

sequence when the p value is less than or equal to about 10^{-2}; more usually; less than or equal to about 10^{-3}; even more usually; less than or equal to about 10^{-4}. More typically, the p value is no more than about 10^{-5}; more typically; no more than or equal to about 10^{-10}; even more typically; no more than or equal to about 10^{-15} for the query sequence to be considered high similarity.

Similarity Determined by Sequence Identity Alone. Sequence identity alone can be used to determine similarity of a query sequence to an individual sequence and can indicate the activity of the sequence. Such an alignment, preferably, permits gaps to align sequences. Typically, the query sequence is related to the profile sequence if the sequence identity over the entire query sequence is at least about 15%; more typically, at least about 20%; even more typically, at least about 25%; even more typically, at least about 50%. Sequence identity alone as a measure of similarity is most useful when the query sequence is usually, at least 80 residues in length; more usually, 90 residues; even more usually, at least 95 amino acid residues in length. More typically, similarity can be concluded based on sequence identity alone when the query sequence is preferably 100 residues in length; more preferably, 120 residues in length; even more preferably, 150 amino acid residues in length.

Alignments with Profile and Multiple Aligned Sequences. Translations of the provided polynucleotides can be aligned with amino acid profiles that define either protein families or common motifs. Also, translations of the provided polynucleotides can be aligned to multiple sequence alignments (MSA) comprising the polypeptide sequences of members of protein families or motifs. Similarity or identity with profile sequences or MSAs can be used to determine the activity of the gene products (*e.g.*, polypeptides) encoded by the provided polynucleotides or corresponding cDNA or genes. For example, sequences that show an identity or similarity with a chemokine profile or MSA can exhibit chemokine activities.

Profiles can be designed manually by (1) creating an MSA, which is an alignment of the amino acid sequence of members that belong to the family and (2) constructing a statistical representation of the alignment. Such methods are described, for example, in Birney et al., *Nucl. Acid Res.* (1996) *24(14)*: 2730-2739. MSAs of some protein families and motifs are publicly available. MSAs are described also in Sonnhammer et al., *Proteins* (1997) *28*: 405-420. A brief description of MSAs is reported in Pascarella et al., *Prot. Eng.* (1996) *9(3)*:249-251. Techniques for building profiles from MSAs are described in Sonnhammer et al., *supra*; Birney et al., *supra*;

and "Computer Methods for Macromolecular Sequence Analysis," *Methods in Enzymology* (1996) *266*, Doolittle, Academic Press, Inc., San Diego, California, USA.

Similarity between a query sequence and a protein family or motif can be determined by (a) comparing the query sequence against the profile and/or (b) aligning the query sequence with the members of the family or motif. Typically, a program such as Searchwise is used to compare the query sequence to the statistical representation of the multiple alignment, also known as a profile (see Birney et al., *supra*). Other techniques to compare the sequence and profile are described in Sonnhammer et al., *supra* and Doolittle, *supra*.

Next, methods described by Feng et al., *J. Mol. Evol.* (1987) 25:351 and Higgins et al., *CABIOS* (1989) *5*:151 can be used align the query sequence with the members of a family or motif, also known as a MSA. Sequence alignments can be generated using any of a variety of software tools. Examples include PileUp, which creates a multiple sequence alignment, and is described in Feng et al., *J. Mol. Evol.* (1987) *25*:351. Another method, GAP, uses the alignment method of Needleman et al., *J. Mol. Biol.* (1970) *48*:443. GAP is best suited for global alignment of sequences. A third method, BestFit, functions by inserting gaps to maximize the number of matches using the local homology algorithm of Smith et al., *Adv. Appl. Math.* (1981) *2*:482. In general, the following factors are used to determine if a similarity between a query sequence and a profile or MSA exists: (1) number of conserved residues found in the query sequence, (2) percentage of conserved residues found in the query sequence, (3) number of frameshifts, and (4) spacing between conserved residues.

Some alignment programs that both translate and align sequences can make any number of frameshifts when translating the nucleotide sequence to produce the best alignment. The fewer frameshifts needed to produce an alignment, the stronger the similarity or identity between the query and profile or MSAs. For example, a weak similarity resulting from no frameshifts can be a better indication of activity or structure of a query sequence, than a strong similarity resulting from two frameshifts. Preferably, three or fewer frameshifts are found in an alignment; more preferably two or fewer frameshifts; even more preferably, one or fewer frameshifts; even more preferably, no frameshifts are found in an alignment of query and profile or MSAs.

Conserved residues are those amino acids found at a particular position in all or some of the family or motif members. Alternatively, a position is considered conserved if only a certain class of amino acids is found in a particular position in all or

some of the family members. For example, the N-terminal position can contain a positively charged amino acid, such as lysine, arginine, or histidine.

Typically, a residue of a polypeptide is conserved when a class of amino acids or a single amino acid is found at a particular position in at least about 40% of all class members; more typically, at least about 50%; even more typically, at least about 60% of the members. Usually, a residue is conserved when a class or single amino acid is found in at least about 70% of the members of a family or motif; more usually, at least about 80%; even more usually, at least about 90%; even more usually, at least about 95%.

A residue is considered conserved when three unrelated amino acids are found at a particular position in the some or all of the members; more usually, two unrelated amino acids. These residues are conserved when the unrelated amino acids are found at particular positions in at least about 40% of all class member; more typically, at least about 50%; even more typically, at least about 60% of the members. Usually, a residue is conserved when a class or single amino acid is found in at least about 70% of the members of a family or motif; more usually, at least about 80%; even more usually, at least about 90%; even more usually, at least about 95%.

A query sequence has similarity to a profile or MSA when the query sequence comprises at least about 25% of the conserved residues of the profile or MSA; more usually, at least about 30%; even more usually; at least about 40%. Typically, the query sequence has a stronger similarity to a profile sequence or MSA when the query sequence comprises at least about 45% of the conserved residues of the profile or MSA; more typically, at least about 50%; even more typically; at least about 55%.

Identification of Secreted and Membrane-Bound Polypeptides

Both secreted and membrane-bound polypeptides of the present invention are of particular interest. For example, levels of secreted polypeptides can be assayed in body fluids that are convenient, such as blood, plasma, serum, and other body fluids such as urine, prostatic fluid and semen. Membrane-bound polypeptides are useful for constructing vaccine antigens or inducing an immune response. Such antigens would comprise all or part of the extracellular region of the membrane-bound polypeptides. Because both secreted and membrane-bound polypeptides comprise a fragment of contiguous hydrophobic amino acids, hydrophobicity predicting algorithms can be used to identify such polypeptides.

A signal sequence is usually encoded by both secreted and membrane-bound polypeptide genes to direct a polypeptide to the surface of the cell. The signal sequence usually comprises a stretch of hydrophobic residues. Such signal sequences can fold into helical structures. Membrane-bound polypeptides typically comprise at least one transmembrane region that possesses a stretch of hydrophobic amino acids that can transverse the membrane. Some transmembrane regions also exhibit a helical structure. Hydrophobic fragments within a polypeptide can be identified by using computer algorithms. Such algorithms include Hopp & Woods, *Proc. Natl. Acad. Sci. USA* (1981) *78*:3824-3828; Kyte & Doolittle, *J. Mol. Biol.* (1982) *157*: 105-132; and RAOAR algorithm, Degli Esposti et al., *Eur. J. Biochem.* (1990) *190*: 207-219.

Another method of identifying secreted and membrane-bound polypeptides is to translate the polynucleotides of the invention in all six frames and determine if at least 8 contiguous hydrophobic amino acids are present. Those translated polypeptides with at least 8; more typically, 10; even more typically, 12 contiguous hydrophobic amino acids are considered to be either a putative secreted or membrane bound polypeptide. Hydrophobic amino acids include alanine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, tryptophan, tyrosine, and valine

Identification of the Function of an Expression Product of a Full-Length Gene

Ribozymes, antisense constructs, and dominant negative mutants can be used to determine function of the expression product of a gene corresponding to a polynucleotide provided herein. The phosphoramidite method of oligonucleotide synthesis can be used to construct antisense molecules and ribozymes. See Beaucage et al., *Tet. Lett.* (1981) *22*:1859 and U.S. Patent No. 4,668,777. Automated devices for synthesis are available to create oligonucleotides using this chemistry. Examples of such devices include Biosearch 8600, Models 392 and 394 by Applied Biosystems, a division of Perkin-Elmer Corp., Foster City, California, USA; and Expedite by Perceptive Biosystems, Framingham, Massachusetts, USA. Synthetic RNA, phosphate analog oligonucleotides, and chemically derivatized oligonucleotides can also be produced, and can be covalently attached to other molecules. RNA oligonucleotides can be synthesized, for example, using RNA phosphoramidites. This method can be performed on an automated synthesizer, such as Applied Biosystems, Models 392 and 394, Foster City, California, USA.

Oligonucleotides of up to 200 nt can be synthesized, more typically, 100 nt, more typically 50 nt; even more typically 30 to 40 nt. These synthetic fragments can be annealed and ligated together to construct larger fragments. See, for example, Sambrook et al., *supra*. Trans-cleaving catalytic RNAs (ribozymes) are RNA molecules possessing endoribonuclease activity. Ribozymes are specifically designed for a particular target, and the target message must contain a specific nucleotide sequence. They are engineered to cleave any RNA species site-specifically in the background of cellular RNA. The cleavage event renders the mRNA unstable and prevents protein expression. Importantly, ribozymes can be used to inhibit expression of a gene of unknown function for the purpose of determining its function in an *in vitro* or *in vivo* context, by detecting the phenotypic effect.

Antisense nucleic acids are designed to specifically bind to RNA, resulting in the formation of RNA-DNA or RNA-RNA hybrids, with an arrest of DNA replication, reverse transcription or messenger RNA translation. Antisense polynucleotides based on a selected polynucleotide sequence can interfere with expression of the corresponding gene. Antisense polynucleotides are typically generated within the cell by expression from antisense constructs that contain the antisense strand as the transcribed strand. Antisense polynucleotides based on the disclosed polynucleotides will bind and/or interfere with the translation of mRNA comprising a sequence complementary to the antisense polynucleotide. The expression products of control cells and cells treated with the antisense construct are compared to detect the protein product of the gene corresponding to the polynucleotide upon which the antisense construct is based. The protein is isolated and identified using routine biochemical methods.

Given the extensive background literature and clinical experience in antisense therapy, one skilled in the art can use selected polynucleotides of the invention as additional potential therapeutics. The choice of polynucleotide can be narrowed by first testing them for binding to "hot spot" regions of the genome of cancerous cells. If a polynucleotide is identified as binding to a "hot spot," testing the polynucleotide as an antisense compound in the corresponding cancer cells is warranted.

Dominant negative mutations also are readily generated for corresponding proteins that are active as homomultimers. A mutant polypeptide will interact with wild-type polypeptides (made from the other allele) and form a non-functional multimer. Thus, a mutation is in a substrate-binding domain, a catalytic

domain, or a cellular localization domain. Preferably, the mutant polypeptide will be overproduced. Point mutations are made that have such an effect. In addition, fusion of different polypeptides of various lengths to the terminus of a protein can yield dominant negative mutants. General strategies are available for making dominant negative mutants (see, *e.g.*, Herskowitz, *Nature* (1987) *329*:219). Such techniques can be used to create loss of function mutations, which are useful for determining protein function.

Polypeptides and Variants Thereof

The polypeptides of the invention include those encoded by the disclosed polynucleotides, as well as nucleic acids that, by virtue of the degeneracy of the genetic code, are not identical in sequence to the disclosed polynucleotides. Thus, the invention includes within its scope a polypeptide encoded by a polynucleotide having the sequence of any one of SEQ ID NOs:1-3351 or a variant thereof.

In general, the term "polypeptide" as used herein refers to both the full length polypeptide encoded by the recited polynucleotide, the polypeptide encoded by the gene represented by the recited polynucleotide, as well as portions or fragments thereof. "Polypeptides" also includes variants of the naturally occurring proteins, where such variants are homologous or substantially similar to the naturally occurring protein, and can be of an origin of the same or different species as the naturally occurring protein (*e.g.*, human, murine, or some other species that naturally expresses the recited polypeptide, usually a mammalian species). In general, variant polypeptides have a sequence that has at least about 80%, usually at least about 90%, and more usually at least about 98% sequence identity with a differentially expressed polypeptide of the invention, as measured by BLAST using the parameters described above. The variant polypeptides can be naturally or non-naturally glycosylated, *i.e.*, the polypeptide has a glycosylation pattern that differs from the glycosylation pattern found in the corresponding naturally occurring protein.

The invention also encompasses homologs of the disclosed polypeptides (or fragments thereof) where the homologs are isolated from other species, *i.e.*, other animal or plant species, where such homologs, usually mammalian species, *e.g.*, rodents, such as mice, rats; domestic animals, *e.g.*, horse, cow, dog, cat; and humans. By "homolog" is meant a polypeptide having at least about 35%, usually at least about 40% and more usually at least about 60% amino acid sequence identity to a particular differentially expressed protein as identified above, where sequence identity is determined using the BLAST algorithm, with the parameters described above.

In general, the polypeptides of the subject invention are provided in a non-naturally occurring environment, *e.g.*, are separated from their naturally occurring environment. In certain embodiments, the subject protein is present in a composition that is enriched for the protein as compared to a control. As such, purified polypeptide is provided, where by purified is meant that the protein is present in a composition that is substantially free of non-differentially expressed polypeptides, where by substantially free is meant that less than 90%, usually less than 60% and more usually less than 50% of the composition is made up of non-differentially expressed polypeptides.

Also within the scope of the invention are variants; variants of polypeptides include mutants, fragments, and fusions. Mutants can include amino acid substitutions, additions or deletions. The amino acid substitutions can be conservative amino acid substitutions or substitutions to eliminate non-essential amino acids, such as to alter a glycosylation site, a phosphorylation site or an acetylation site, or to minimize misfolding by substitution or deletion of one or more cysteine residues that are not necessary for function. Conservative amino acid substitutions are those that preserve the general charge, hydrophobicity/ hydrophilicity, and/or steric bulk of the amino acid substituted. Variants can be designed so as to retain biological activity of a particular region of the protein (*e.g.*, a functional domain and/or, where the polypeptide is a member of a protein family, a region associated with a consensus sequence). Selection of amino acid alterations for production of variants can be based upon the accessibility (interior vs. exterior) of the amino acid (see, *e.g.*, Go et al., *Int. J. Peptide Protein Res.* (1980) *15*:211), the thermostability of the variant polypeptide (see, *e.g.*, Querol et al., *Prot. Eng.* (1996) *9*:265), desired glycosylation sites (see, *e.g.*, Olsen and Thomsen, J. *Gen. Microbiol.* (1991) *137*:579), desired disulfide bridges (see, *e.g.*, Clarke et al., *Biochemistry* (1993) *32*:4322; and Wakarchuk et al., *Protein Eng.* (1994) *7*:1379), desired metal binding sites (see, *e.g.*, Toma et al., *Biochemistry* (1991) *30*:97, and Haezerbrouck et al., *Protein Eng.* (1993) *6*:643), and desired substitutions with in proline loops (see, *e.g.*, Masul et al., *Appl. Env. Microbiol.* (1994) *60*:3579). Cysteine-depleted muteins can be produced as disclosed in U.S. Patent No. 4,959,314.

Variants also include fragments of the polypeptides disclosed herein, particularly biologically active fragments and/or fragments corresponding to functional domains. Fragments of interest will typically be at least about 10 aa to at least about 15 aa in length, usually at least about 50 aa in length, and can be as long as 300 aa in length or longer, but will usually not exceed about 1000 aa in length, where the fragment will have a stretch of amino acids that is identical to a polypeptide encoded by a

polynucleotide having a sequence of any SEQ ID NOs:1-3351, or a homolog thereof. The protein variants described herein are encoded by polynucleotides that are within the scope of the invention. The genetic code can be used to select the appropriate codons to construct the corresponding variants.

Computer-Related Embodiments

In general, a library of polynucleotides is a collection of sequence information, which information is provided in either biochemical form (*e.g.*, as a collection of polynucleotide molecules), or in electronic form (*e.g.*, as a collection of polynucleotide sequences stored in a computer-readable form, as in a computer system and/or as part of a computer program). The sequence information of the polynucleotides can be used in a variety of ways, *e.g.*, as a resource for gene discovery, as a representation of sequences expressed in a selected cell type (*e.g.*, cell type markers), and/or as markers of a given disease or disease state. In general, a disease marker is a representation of a gene product that is present in all cells affected by disease either at an increased or decreased level relative to a normal cell (*e.g.*, a cell of the same or similar type that is not substantially affected by disease). For example, a polynucleotide sequence in a library can be a polynucleotide that represents an mRNA, polypeptide, or other gene product encoded by the polynucleotide, that is either overexpressed or underexpressed in a breast ductal cell affected by cancer relative to a normal (*i.e.*, substantially disease-free) breast cell.

The nucleotide sequence information of the library can be embodied in any suitable form, *e.g.*, electronic or biochemical forms. For example, a library of sequence information embodied in electronic form comprises an accessible computer data file (or, in biochemical form, a collection of nucleic acid molecules) that contains the representative nucleotide sequences of genes that are differentially expressed (*e.g.*, overexpressed or underexpressed) as between, for example, i) a cancerous cell and a normal cell; ii) a cancerous cell and a dysplastic cell; iii) a cancerous cell and a cell affected by a disease or condition other than cancer; iv) a metastatic cancerous cell and a normal cell and/or non-metastatic cancerous cell; v) a malignant cancerous cell and a non-malignant cancerous cell (or a normal cell) and/or vi) a dysplastic cell relative to a normal cell. Other combinations and comparisons of cells affected by various diseases or stages of disease will be readily apparent to the ordinarily skilled artisan. Biochemical embodiments of the library include a collection of nucleic acids that have

the sequences of the genes in the library, where the nucleic acids can correspond to the entire gene in the library or to a fragment thereof, as described in greater detail below.

The polynucleotide libraries of the subject invention generally comprise sequence information of a plurality of polynucleotide sequences, where at least one of the polynucleotides has a sequence of any of SEQ ID NOs:1-3351. By plurality is meant at least 2, usually at least 3 and can include up to all of SEQ ID NOs:1-3351. The length and number of polynucleotides in the library will vary with the nature of the library, *e.g.*, if the library is an oligonucleotide array, a cDNA array, a computer database of the sequence information, *etc.*

Where the library is an electronic library, the nucleic acid sequence information can be present in a variety of media. "Media" refers to a manufacture, other than an isolated nucleic acid molecule, that contains the sequence information of the present invention. Such a manufacture provides the genome sequence or a subset thereof in a form that can be examined by means not directly applicable to the sequence as it exists in a nucleic acid. For example, the nucleotide sequence of the present invention, *e.g.*, the nucleic acid sequences of any of the polynucleotides of SEQ ID NOs:1-3351, can be recorded on computer readable media, *e.g.*, any medium that can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as a floppy disc, a hard disc storage medium, and a magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. One of skill in the art can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising a recording of the present sequence information. "Recorded" refers to a process for storing information on computer readable medium, using any such methods as known in the art. Any convenient data storage structure can be chosen, based on the means used to access the stored information. A variety of data processor programs and formats can be used for storage, *e.g.*, word processing text file, database format, *etc.* In addition to the sequence information, electronic versions of the libraries of the invention can be provided in conjunction or connection with other computer-readable information and/or other types of computer-readable files (*e.g.*, searchable files, executable files, *etc.*, including, but not limited to, for example, search program software, *etc.*).

By providing the nucleotide sequence in computer readable form, the information can be accessed for a variety of purposes. Computer software to access sequence information is publicly available. For example, the BLAST (Altschul et al.,

supra.) and BLAZE (Brutlag et al. *Comp. Chem.* (1993) *17*:203) search algorithms on a Sybase system can be used to identify open reading frames (ORFs) within the genome that contain homology to ORFs from other organisms.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based system are suitable for use in the present invention. The data storage means can comprise any manufacture comprising a recording of the present sequence information as described above, or a memory access means that can access such a manufacture.

"Search means" refers to one or more programs implemented on the computer-based system, to compare a target sequence or target structural motif, or expression levels of a polynucleotide in a sample, with the stored sequence information. Search means can be used to identify fragments or regions of the genome that match a particular target sequence or target motif. A variety of known algorithms are publicly known and commercially available, *e.g.*, MacPattern (EMBL), BLASTN and BLASTX (NCBI). A "target sequence" can be any polynucleotide or amino acid sequence of six or more contiguous nucleotides or two or more amino acids, preferably from about 10 to 100 amino acids or from about 30 to 300 nt. A variety of comparing means can be used to accomplish comparison of sequence information from a sample (*e.g.*, to analyze target sequences, target motifs, or relative expression levels) with the data storage means. A skilled artisan can readily recognize that any one of the publicly available homology search programs can be used as the search means for the computer based systems of the present invention to accomplish comparison of target sequences and motifs. Computer programs to analyze expression levels in a sample and in controls are also known in the art.

A "target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration that is formed upon the folding of the target motif, or on consensus sequences of regulatory or active sites. There are a variety of target motifs known in the art. Protein target motifs include, but arc not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are

not limited to, hairpin structures, promoter sequences and other expression elements such as binding sites for transcription factors.

A variety of structural formats for the input and output means can be used to input and output the information in the computer-based systems of the present invention. One format for an output means ranks the relative expression levels of different polynucleotides. Such presentation provides a skilled artisan with a ranking of relative expression levels to determine a gene expression profile.

As discussed above, the "library" of the invention also encompasses biochemical libraries of the polynucleotides of SEQ ID NOs:1-3351, *e.g.*, collections of nucleic acids representing the provided polynucleotides. The biochemical libraries can take a variety of forms, *e.g.*, a solution of cDNAs, a pattern of probe nucleic acids stably associated with a surface of a solid support (*i.e.*, an array) and the like. Of particular interest are nucleic acid arrays in which one or more of SEQ ID NOs:1-3351 is represented on the array. By array is meant an article of manufacture that has at least a substrate with at least two distinct nucleic acid targets on one of its surfaces, where the number of distinct nucleic acids can be considerably higher, typically being at least 10 nt, usually at least 20 nt and often at least 25 nt. A variety of different array formats have been developed and are known to those of skill in the art. The arrays of the subject invention find use in a variety of applications, including gene expression analysis, drug screening, mutation analysis and the like, as disclosed in the above-listed exemplary patent documents.

In addition to the above nucleic acid libraries, analogous libraries of polypeptides are also provided, where the where the polypeptides of the library will represent at least a portion of the polypeptides encoded by SEQ ID NOs:1-3351.

<u>Use of Polynucleotide Probes in Mapping, and in Tissue Profiling</u>

Polynucleotide probes, generally comprising at least 12 contiguous nt of a polynucleotide as shown in the Sequence Listing, are used for a variety of purposes, such as chromosome mapping of the polynucleotide and detection of transcription levels. Additional disclosure about preferred regions of the disclosed polynucleotide sequences is found in the Examples. A probe that hybridizes specifically to a polynucleotide disclosed herein should provide a detection signal at least 5-, 10-, or 20-fold higher than the background hybridization provided with other unrelated sequences.

<u>Detection of Expression Levels</u>. Nucleotide probes are used to detect expression of a gene corresponding to the provided polynucleotide. In Northern blots,

mRNA is separated electrophoretically and contacted with a probe. A probe is detected as hybridizing to an mRNA species of a particular size. The amount of hybridization is quantitated to determine relative amounts of expression, for example under a particular condition. Probes are used for *in situ* hybridization to cells to detect expression. Probes can also be used *in vivo* for diagnostic detection of hybridizing sequences. Probes are typically labeled with a radioactive isotope. Other types of detectable labels can be used such as chromophores, fluors, and enzymes. Other examples of nucleotide hybridization assays are described in WO92/02526 and U.S. Patent No. 5,124,246.

Alternatively, the Polymerase Chain Reaction (PCR) is another means for detecting small amounts of target nucleic acids (see, *e.g.*, Mullis et al., *Meth. Enzymol.* (1987) *155*:335; U.S. Patent No. 4,683,195; and U.S. Patent No. 4,683,202). Two primer polynucleotides nucleotides that hybridize with the target nucleic acids are used to prime the reaction. The primers can be composed of sequence within or 3' and 5' to the polynucleotides of the Sequence Listing. Alternatively, if the primers are 3' and 5' to these polynucleotides, they need not hybridize to them or the complements. After amplification of the target with a thermostable polymerase, the amplified target nucleic acids can be detected by methods known in the art, *e.g.*, Southern blot. mRNA or cDNA can also be detected by traditional blotting techniques (*e.g.*, Southern blot, Northern blot, *etc.*) described in Sambrook et al., "Molecular Cloning: A Laboratory Manual" (New York, Cold Spring Harbor Laboratory, 1989) (*e.g.*, without PCR amplification). In general, mRNA or cDNA generated from mRNA using a polymerase enzyme can be purified and separated using gel electrophoresis, and transferred to a solid support, such as nitrocellulose. The solid support is exposed to a labeled probe, washed to remove any unhybridized probe, and duplexes containing the labeled probe are detected.

Mapping. Polynucleotides of the present invention can be used to identify a chromosome on which the corresponding gene resides. Such mapping can be useful in identifying the function of the polynucleotide-related gene by its proximity to other genes with known function. Function can also be assigned to the polynucleotide-related gene when particular syndromes or diseases map to the same chromosome. For example, use of polynucleotide probes in identification and quantification of nucleic acid sequence aberrations is described in U.S. Patent No. 5,783,387. An exemplary mapping method is fluorescence *in situ* hybridization (FISH), which facilitates comparative genomic hybridization to allow total genome assessment of changes in relative copy number of DNA sequences (see, *e.g.*, Valdes et al., *Methods in Molecular*

Biology (1997) *68*:1). Polynucleotides can also be mapped to particular chromosomes using, for example, radiation hybrids or chromosome-specific hybrid panels. See Leach et al., *Advances in Genetics*, (1995) *33*:63-99; Walter et al., *Nature Genetics* (1994) *7*:22; Walter and Goodfellow, *Trends in Genetics* (1992) *9*:352. Panels for radiation hybrid mapping are available from Research Genetics, Inc., Huntsville, Alabama, USA. The statistical program RHMAP can be used to construct a map based on the data from radiation hybridization with a measure of the relative likelihood of one order versus another. RHMAP is available via the world wide web at http://www.sph.umich.edu-/group/statgen/software. In addition, commercial programs are available for identifying regions of chromosomes commonly associated with disease, such as cancer.

Tissue Typing or Profiling. Expression of specific mRNA corresponding to the provided polynucleotides can vary in different cell types and can be tissue-specific. This variation of mRNA levels in different cell types can be exploited with nucleic acid probe assays to determine tissue types. For example, PCR, branched DNA probe assays, or blotting techniques utilizing nucleic acid probes substantially identical or complementary to polynucleotides listed in the Sequence Listing can determine the presence or absence of the corresponding cDNA or mRNA.

Tissue typing can be used to identify the developmental organ or tissue source of a metastatic lesion by identifying the expression of a particular marker of that organ or tissue. If a polynucleotide is expressed only in a specific tissue type, and a metastatic lesion is found to express that polynucleotide, then the developmental source of the lesion has been identified. Expression of a particular polynucleotide can be assayed by detection of either the corresponding mRNA or the protein product.

Use of Polymorphisms. A polynucleotide of the invention can be used in forensics, genetic analysis, mapping, and diagnostic applications where the corresponding region of a gene is polymorphic in the human population. Any means for detecting a polymorphism in a gene can be used, including, but not limited to electrophoresis of protein polymorphic variants, differential sensitivity to restriction enzyme cleavage, and hybridization to allele-specific probes.

Antibody Production

Expression products of a polynucleotide of the invention, as well as the corresponding mRNA, cDNA, or complete gene, can be prepared and used for raising antibodies for experimental, diagnostic, and therapeutic purposes. For polynucleotides to which a corresponding gene has not been assigned, this provides an additional

method of identifying the corresponding gene. The polynucleotide or related cDNA is expressed as described above, and antibodies are prepared. These antibodies are specific to an epitope on the polypeptide encoded by the polynucleotide, and can precipitate or bind to the corresponding native protein in a cell or tissue preparation or in a cell-free extract of an *in vitro* expression system.

Methods for production of monoclonal and polyclonal antibodies that specifically bind a selected antigen are well known in the art. The antibodies specifically bind to epitopes present in the polypeptides encoded by polynucleotides disclosed in the Sequence Listing. Typically, at least 6, 8, 10, or 12 contiguous amino acids are required to form an epitope. Epitopes that involve non-contiguous amino acids may require a longer polypeptide, *e.g.*, at least 15, 25, or 50 amino acids. Antibodies that specifically bind to human polypeptides encoded by the provided polynucleotides should provide a detection signal at least 5-, 10-, or 20-fold higher than a detection signal provided with other proteins when used in Western blots or other immunochemical assays. Preferably, antibodies that specifically polypeptides of the invention do not bind to other proteins in immunochemical assays at detectable levels and can immunoprecipitate the specific polypeptide from solution.

The invention also contemplates naturally occurring antibodies specific for a polypeptide of the invention. For example, serum antibodies to a polypeptide of the invention in a human population can be purified by methods well known in the art, *e.g.*, by passing antiserum over a column to which the corresponding selected polypeptide or fusion protein is bound. The bound antibodies can then be eluted from the column, for example using a buffer with a high salt concentration.

In addition to the antibodies discussed above, the invention also contemplates genetically engineered antibodies, antibody derivatives (*e.g.*, single chain antibodies, antibody fragments (*e.g.*, Fab, *etc.*)), according to methods well known in the art.

Other embodiments of the present invention include humanized monoclonal antibodies capable of binding to the polypeptides of the invention. The phrase "humanized antibody" refers to an antibody derived from a non-human antibody - typically a mouse monoclonal antibody. Alternatively, a humanized antibody may be derived from a chimeric antibody that retains or substantially retains the antigen-binding properties of the parental, non-human, antibody but which exhibits diminished immunogenicity as compared to the parental antibody when administered to humans. The phrase "chimeric antibody," as used herein, refers to an antibody containing

sequence derived from two different antibodies (*see, e.g.*, U.S. Patent No. 4,816,567) which typically originate from different species. Most typically, chimeric antibodies comprise human and murine antibody fragments, generally human constant and mouse variable regions.

Because humanized antibodies are far less immunogenic in humans than the parental mouse monoclonal antibodies, they can be used for the treatment of humans with far less risk of anaphylaxis. Thus, these antibodies may be preferred in therapeutic applications that involve *in vivo* administration to a human such as, *e.g.*, use as radiation sensitizers for the treatment of neoplastic disease or use in methods to reduce the side effects of, *e.g.*, cancer therapy.

Humanized antibodies may be achieved by a variety of methods including, for example: (1) grafting the non-human complementarity determining regions (CDRs) onto a human framework and constant region (a process referred to in the art as "humanizing"), or, alternatively, (2) transplanting the entire non-human variable domains, but "cloaking" them with a human-like surface by replacement of surface residues (a process referred to in the art as "veneering"). In the present invention, humanized antibodies will include both "humanized" and "veneered" antibodies. These methods are disclosed in, *e.g.*, Jones et al., *Nature 321*:522-525 (1986); Morrison et al., *Proc. Natl. Acad. Sci., U.S.A.*, *81*:6851-6855 (1984); Morrison and Oi, *Adv. Immunol.*, *44*:65-92 (1988); Verhoeyer et al., *Science 239*:1534-1536 (1988); Padlan, *Molec. Immun. 28*:489-498 (1991); Padlan, *Molec. Immunol. 31(3)*:169-217 (1994); and Kettleborough, C.A. et al., *Protein Eng. 4(7)*:773-83 (1991) each of which is incorporated herein by reference.

The phrase "complementarity determining region" refers to amino acid sequences which together define the binding affinity and specificity of the natural Fv region of a native immunoglobulin binding site. *See, e.g.*, Chothia et al., *J. Mol. Biol. 196*:901-917 (1987); Kabat et al., U.S. Dept. of Health and Human Services NIH Publication No. 91-3242 (1991). The phrase "constant region" refers to the portion of the antibody molecule that confers effector functions. In the present invention, mouse constant regions are substituted by human constant regions. The constant regions of the subject humanized antibodies are derived from human immunoglobulins. The heavy chain constant region can be selected from any of the five isotypes: alpha, delta, epsilon, gamma or mu.

One method of humanizing antibodies comprises aligning the non-human heavy and light chain sequences to human heavy and light chain sequences,

selecting and replacing the non-human framework with a human framework based on such alignment, molecular modeling to predict the conformation of the humanized sequence and comparing to the conformation of the parent antibody. This process is followed by repeated back mutation of residues in the CDR region which disturb the structure of the CDRs until the predicted conformation of the humanized sequence model closely approximates the conformation of the non-human CDRs of the parent non-human antibody. Such humanized antibodies may be further derivatized to facilitate uptake and clearance, *e.g.*, via Ashwell receptors. *See, e.g.,* U.S. Patent Nos. 5,530,101 and 5,585,089 which patents are incorporated herein by reference.

Humanized antibodies can also be produced using transgenic animals that are engineered to contain human immunoglobulin loci. For example, WO 98/24893 discloses transgenic animals having a human Ig locus wherein the animals do not produce functional endogenous immunoglobulins due to the inactivation of endogenous heavy and light chain loci. WO 91/10741 also discloses transgenic non-primate mammalian hosts capable of mounting an immune response to an immunogen, wherein the antibodies have primate constant and/or variable regions, and wherein the endogenous immunoglobulin-encoding loci are substituted or inactivated. WO 96/30498 discloses the use of the Cre/Lox system to modify the immunoglobulin locus in a mammal, such as to replace all or a portion of the constant or variable region to form a modified antibody molecule. WO 94/02602 discloses non-human mammalian hosts having inactivated endogenous Ig loci and functional human Ig loci. U.S. Patent No. 5,939,598 discloses methods of making transgenic mice in which the mice lack endogenous heavy claims, and express an exogenous immunoglobulin locus comprising one or more xenogeneic constant regions.

Using a transgenic animal described above, an immune response can be produced to a selected antigenic molecule, and antibody-producing cells can be removed from the animal and used to produce hybridomas that secrete human monoclonal antibodies. Immunization protocols, adjuvants, and the like are known in the art, and are used in immunization of, for example, a transgenic mouse as described in WO 96/33735. This publication discloses monoclonal antibodies against a variety of antigenic molecules including IL-6, IL-8, TNF , human CD4, L-selectin, gp39, and tetanus toxin. The monoclonal antibodies can be tested for the ability to inhibit or neutralize the biological activity or physiological effect of the corresponding protein. WO 96/33735 discloses that monoclonal antibodies against IL-8, derived from immune cells of transgenic mice immunized with IL-8, blocked IL-8-induced functions of

neutrophils. Human monoclonal antibodies with specificity for the antigen used to immunize transgenic animals are also disclosed in WO 96/34096.

Polynucleotides or Arrays for Diagnostics

Polynucleotide arrays are created by spotting polynucleotide probes onto a substrate (*e.g.*, glass, nitrocellose, *etc.*) in a two-dimensional matrix or array having bound probes. The probes can be bound to the substrate by either covalent bonds or by non-specific interactions, such as hydrophobic interactions. Samples of polynucleotides can be detectably labeled (*e.g.*, using radioactive or fluorescent labels) and then hybridized to the probes. Double stranded polynucleotides, comprising the labeled sample polynucleotides bound to probe polynucleotides, can be detected once the unbound portion of the sample is washed away. Techniques for constructing arrays and methods of using these arrays are described in EP 799 897; WO 97/29212; WO 97/27317; EP 785 280; WO 97/02357; U.S. Patent No. 5,593,839; U.S. Patent No. 5,578,832; EP 728 520; U.S. Patent No. 5,599,695; EP 721 016; U.S. Patent No. 5,556,752; WO 95/22058; and U.S. Patent No. 5,631,734. Arrays can be used to, for example, examine differential expression of genes and can be used to determine gene function. For example, arrays can be used to detect differential expression of a polynucleotide between a test cell and control cell (*e.g.*, cancer cells and normal cells). For example, high expression of a particular message in a cancer cell, which is not observed in a corresponding normal cell, can indicate a cancer specific gene product. Exemplary uses of arrays are further described in, for example, Pappalarado et al., *Sem. Radiation Oncol.* (1998) *8*:217; and Ramsay, *Nature Biotechnol.* (1998) *16*:40.

Differential Expression in Diagnosis

The polynucleotides of the invention can also be used to detect differences in expression levels between two cells, *e.g.*, as a method to identify abnormal or diseased tissue in a human. For polynucleotides corresponding to profiles of protein families, the choice of tissue can be selected according to the putative biological function. In general, the expression of a gene corresponding to a specific polynucleotide is compared between a first tissue that is suspected of being diseased and a second, normal tissue of the human. The tissue suspected of being abnormal or diseased can be derived from a different tissue type of the human, but preferably it is derived from the same tissue type; for example an intestinal polyp or other abnormal growth should be compared with normal intestinal tissue. The normal tissue can be the

same tissue as that of the test sample, or any normal tissue of the patient, especially those that express the polynucleotide-related gene of interest (*e.g.*, brain, thymus, testis, heart, prostate, placenta, spleen, small intestine, skeletal muscle, pancreas, and the mucosal lining of the colon). A difference between the polynucleotide-related gene, mRNA, or protein in the two tissues which are compared, for example in molecular weight, amino acid or nucleotide sequence, or relative abundance, indicates a change in the gene, or a gene which regulates it, in the tissue of the human that was suspected of being diseased. Examples of detection of differential expression and its use in diagnosis of cancer are described in U.S. Patent Nos. 5,688,641 and 5,677,125.

A genetic predisposition to disease in a human can also be detected by comparing expression levels of an mRNA or protein corresponding to a polynucleotide of the invention in a fetal tissue with levels associated in normal fetal tissue. Fetal tissues that are used for this purpose include, but are not limited to, amniotic fluid, chorionic villi, blood, and the blastomere of an *in vitro*-fertilized embryo. The comparable normal polynucleotide-related gene is obtained from any tissue. The mRNA or protein is obtained from a normal tissue of a human in which the polynucleotide-related gene is expressed. Differences such as alterations in the nucleotide sequence or size of the same product of the fetal polynucleotide-related gene or mRNA, or alterations in the molecular weight, amino acid sequence, or relative abundance of fetal protein, can indicate a germline mutation in the polynucleotide-related gene of the fetus, which indicates a genetic predisposition to disease. In general, diagnostic, prognostic, and other methods of the invention based on differential expression involve detection of a level or amount of a gene product, particularly a differentially expressed gene product, in a test sample obtained from a patient suspected of having or being susceptible to a disease (*e.g.*, breast cancer, lung cancer, colon cancer and/or metastatic forms thereof), and comparing the detected levels to those levels found in normal cells (*e.g.*, cells substantially unaffected by cancer) and/or other control cells (*e.g.*, to differentiate a cancerous cell from a cell affected by dysplasia). Furthermore, the severity of the disease can be assessed by comparing the detected levels of a differentially expressed gene product with those levels detected in samples representing the levels of differentially gene product associated with varying degrees of severity of disease. It should be noted that use of the term "diagnostic" herein is not necessarily meant to exclude "prognostic" or "prognosis," but rather is used as a matter of convenience.

The term "differentially expressed gene" is generally intended to encompass a polynucleotide that can, for example, include an open reading frame

encoding a gene product (*e.g.*, a polypeptide), and/or introns of such genes and adjacent 5' and 3' non-coding nucleotide sequences involved in the regulation of expression, up to about 20 kb beyond the coding region, but possibly further in either direction. The gene can be introduced into an appropriate vector for extrachromosomal maintenance or for integration into a host genome. In general, a difference in expression level associated with a decrease in expression level of at least about 25%, usually at least about 50% to 75%, more usually at least about 90% or more is indicative of a differentially expressed gene of interest, *i.e.*, a gene that is underexpressed or down-regulated in the test sample relative to a control sample. Furthermore, a difference in expression level associated with an increase in expression of at least about 25%, usually at least about 50% to 75%, more usually at least about 90% and can be at least about 1 ½-fold, usually at least about 2-fold to about 10-fold, and can be about 100-fold to about 1,000-fold increase relative to a control sample is indicative of a differentially expressed gene of interest, *i.e.*, an overexpressed or up-regulated gene.

"Differentially expressed polynucleotide" as used herein means a nucleic acid molecule (RNA or DNA) comprising a sequence that represents a differentially expressed gene, *e.g.*, the differentially expressed polynucleotide comprises a sequence (*e.g.*, an open reading frame encoding a gene product) that uniquely identifies a differentially expressed gene so that detection of the differentially expressed polynucleotide in a sample is correlated with the presence of a differentially expressed gene in a sample. "Differentially expressed polynucleotides" is also meant to encompass fragments of the disclosed polynucleotides, *e.g.*, fragments retaining biological activity, as well as nucleic acids homologous, substantially similar, or substantially identical (*e.g.*, having about 90% sequence identity) to the disclosed polynucleotides.

"Diagnosis" as used herein generally includes determination of a subject's susceptibility to a disease or disorder, determination as to whether a subject is presently affected by a disease or disorder, as well as to the prognosis of a subject affected by a disease or disorder (*e.g.*, identification of pre-metastatic or metastatic cancerous states, stages of cancer, or responsiveness of cancer to therapy). The present invention particularly encompasses diagnosis of subjects in the context of breast cancer (*e.g.*, carcinoma *in situ* (*e.g.*, ductal carcinoma *in situ*), estrogen receptor (ER)-positive breast cancer, ER-negative breast cancer, or other forms and/or stages of breast cancer), lung cancer (*e.g.*, small cell carcinoma, non-small cell carcinoma, mesothelioma, and

other forms and/or stages of lung cancer), and colon cancer (*e.g.*, adenomatous polyp, colorectal carcinoma, and other forms and/or stages of colon cancer).

"Sample" or "biological sample" as used throughout here are generally meant to refer to samples of biological fluids or tissues, particularly samples obtained from tissues, especially from cells of the type associated with the disease for which the diagnostic application is designed (*e.g.*, ductal adenocarcinoma), and the like. "Samples" is also meant to encompass derivatives and fractions of such samples (*e.g.*, cell lysates). Where the sample is solid tissue, the cells of the tissue can be dissociated or tissue sections can be analyzed.

Methods of the subject invention useful in diagnosis or prognosis typically involve comparison of the abundance of a selected differentially expressed gene product in a sample of interest with that of a control to determine any relative differences in the expression of the gene product, where the difference can be measured qualitatively and/or quantitatively. Quantitation can be accomplished, for example, by comparing the level of expression product detected in the sample with the amounts of product present in a standard curve. A comparison can be made visually; by using a technique such as densitometry, with or without computerized assistance; by preparing a representative library of cDNA clones of mRNA isolated from a test sample, sequencing the clones in the library to determine that number of cDNA clones corresponding to the same gene product, and analyzing the number of clones corresponding to that same gene product relative to the number of clones of the same gene product in a control sample; or by using an array to detect relative levels of hybridization to a selected sequence or set of sequences, and comparing the hybridization pattern to that of a control. The differences in expression are then correlated with the presence or absence of an abnormal expression pattern. A variety of different methods for determining the nucleic acid abundance in a sample are known to those of skill in the art (see, *e.g.*, WO 97/27317).In general, diagnostic assays of the invention involve detection of a gene product of a the polynucleotide sequence (*e.g.*, mRNA or polypeptide) that corresponds to a sequence of SEQ ID NOs:1-3351. The patient from whom the sample is obtained can be apparently healthy, susceptible to disease (*e.g.*, as determined by family history or exposure to certain environmental factors), or can already be identified as having a condition in which altered expression of a gene product of the invention is implicated.

Diagnosis can be determined based on detected gene product expression levels of a gene product encoded by at least one, preferably at least two or more, at least

3 or more, or at least 4 or more of the polynucleotides having a sequence set forth in SEQ ID NOs:1-3351, and can involve detection of expression of genes corresponding to all of SEQ ID NOs:1-3351 and/or additional sequences that can serve as additional diagnostic markers and/or reference sequences. Where the diagnostic method is designed to detect the presence or susceptibility of a patient to cancer, the assay preferably involves detection of a gene product encoded by a gene corresponding to a polynucleotide that is differentially expressed in cancer. Examples of such differentially expressed polynucleotides are described in the Examples below. Given the provided polynucleotides and information regarding their relative expression levels provided herein, assays using such polynucleotides and detection of their expression levels in diagnosis and prognosis will be readily apparent to the ordinarily skilled artisan.

Any of a variety of detectable labels can be used in connection with the various embodiments of the diagnostic methods of the invention. Suitable detectable labels include fluorochromes, (*e.g.*, fluorescein isothiocyanate (FITC), rhodamine, Texas Red, phycoerythrin, allophycocyanin, 6-carboxyfluorescein (6-FAM), 2',7'-dimethoxy-4',5'-dichloro-6-carboxyfluorescein, 6-carboxy-X-rhodamine (ROX), 6-carboxy-2',4',7',4,7-hexachlorofluorescein (HEX), 5-carboxyfluorescein (5-FAM) or N,N,N',N'-tetramethyl-6-carboxyrhodamine (TAMRA)), radioactive labels, (*e.g.*, ^{32}P, ^{35}S, ^{3}H, *etc.*), and the like. The detectable label can involve a two stage systems (*e.g.*, biotin-avidin, hapten-anti-hapten antibody, *etc.*)

Reagents specific for the polynucleotides and polypeptides of the invention, such as antibodies and nucleotide probes, can be supplied in a kit for detecting the presence of an expression product in a biological sample. The kit can also contain buffers or labeling components, as well as instructions for using the reagents to detect and quantify expression products in the biological sample. Exemplary embodiments of the diagnostic methods of the invention are described below in more detail.

Polypeptide detection in diagnosis. In one embodiment, the test sample is assayed for the level of a differentially expressed polypeptide. Diagnosis can be accomplished using any of a number of methods to determine the absence or presence or altered amounts of the differentially expressed polypeptide in the test sample. For example, detection can utilize staining of cells or histological sections with labeled antibodies, performed in accordance with conventional methods. Cells can be permeabilized to stain cytoplasmic molecules. In general, antibodies that specifically bind a differentially expressed polypeptide of the invention are added to a sample, and

incubated for a period of time sufficient to allow binding to the epitope, usually at least about 10 minutes. The antibody can be detectably labeled for direct detection (*e.g.*, using radioisotopes, enzymes, fluorescers, chemiluminescers, and the like), or can be used in conjunction with a second stage antibody or reagent to detect binding (*e.g.*, biotin with horseradish peroxidase-conjugated avidin, a secondary antibody conjugated to a fluorescent compound, *e.g.*, fluorescein, rhodamine, Texas red, *etc.*). The absence or presence of antibody binding can be determined by various methods, including flow cytometry of dissociated cells, microscopy, radiography, scintillation counting, *etc.* Any suitable alternative methods can of qualitative or quantitative detection of levels or amounts of differentially expressed polypeptide can be used, for example ELISA, western blot, immunoprecipitation, radioimmunoassay, *etc.*

mRNA detection. The diagnostic methods of the invention can also or alternatively involve detection of mRNA encoded by a gene corresponding to a differentially expressed polynucleotides of the invention. Any suitable qualitative or quantitative methods known in the art for detecting specific mRNAs can be used. mRNA can be detected by, for example, *in situ* hybridization in tissue sections, by reverse transcriptase-PCR, or in Northern blots containing poly A+ mRNA. One of skill in the art can readily use these methods to determine differences in the size or amount of mRNA transcripts between two samples. mRNA expression levels in a sample can also be determined by generation of a library of expressed sequence tags (ESTs) from the sample, where the EST library is representative of sequences present in the sample (Adams, et al., (1991) Science 252:1651). Enumeration of the relative representation of ESTs within the library can be used to approximate the relative representation of the gene transcript within the starting sample. The results of EST analysis of a test sample can then be compared to EST analysis of a reference sample to determine the relative expression levels of a selected polynucleotide, particularly a polynucleotide corresponding to one or more of the differentially expressed genes described herein. Alternatively, gene expression in a test sample can be performed using serial analysis of gene expression (SAGE) methodology (*e.g.*, Velculescu et al., *Science* (1995) *270*:484) or differential display (DD) methodology (see, *e.g.*, U.S. Patent NOs. 5,776,683 and 5,807,680).

Alternatively, gene expression can be analyzed using hybridization analysis. Oligonucleotides or cDNA can be used to selectively identify or capture DNA or RNA of specific sequence composition, and the amount of RNA or cDNA hybridized to a known capture sequence determined qualitatively or quantitatively, to provide

information about the relative representation of a particular message within the pool of cellular messages in a sample. Hybridization analysis can be designed to allow for concurrent screening of the relative expression of hundreds to thousands of genes by using, for example, array-based technologies having high density formats, including filters, microscope slides, or microchips, or solution-based technologies that use spectroscopic analysis (*e.g.*, mass spectrometry). One exemplary use of arrays in the diagnostic methods of the invention is described below in more detail.

Use of a single gene in diagnostic applications. The diagnostic methods of the invention can focus on the expression of a single differentially expressed gene. For example, the diagnostic method can involve detecting a differentially expressed gene, or a polymorphism of such a gene (*e.g.*, a polymorphism in an coding region or control region), that is associated with disease. Disease-associated polymorphisms can include deletion or truncation of the gene, mutations that alter expression level and/or affect activity of the encoded protein, *etc.*

A number of methods are available for analyzing nucleic acids for the presence of a specific sequence, *e.g.*, a disease associated polymorphism. Where large amounts of DNA are available, genomic DNA is used directly. Alternatively, the region of interest is cloned into a suitable vector and grown in sufficient quantity for analysis. Cells that express a differentially expressed gene can be used as a source of mRNA, which can be assayed directly or reverse transcribed into cDNA for analysis. The nucleic acid can be amplified by conventional techniques, such as the polymerase chain reaction (PCR), to provide sufficient amounts for analysis, and a detectable label can be included in the amplification reaction (*e.g.*, using a detectably labeled primer or detectably labeled oligonucleotides) to facilitate detection. Alternatively, various methods are also known in the art that utilize oligonucleotide ligation as a means of detecting polymorphisms, see *e.g.*, Riley et al., *Nucl. Acids Res.* (1990) *18*:2887; and Delahunty et al., *Am. J. Hum. Genet.* (1996) *58*:1239.

The amplified or cloned sample nucleic acid can be analyzed by one of a number of methods known in the art. The nucleic acid can be sequenced by dideoxy or other methods, and the sequence of bases compared to a selected sequence, *e.g.*, to a wild-type sequence. Hybridization with the polymorphic or variant sequence can also be used to determine its presence in a sample (*e.g.*, by Southern blot, dot blot, *etc.*). The hybridization pattern of a polymorphic or variant sequence and a control sequence to an array of oligonucleotide probes immobilized on a solid support, as described in U.S. Patent No. 5,445,934, or in WO 95/35505, can also be used as a means of identifying

polymorphic or variant sequences associated with disease. Single strand conformational polymorphism (SSCP) analysis, denaturing gradient gel electrophoresis (DGGE), and heteroduplex analysis in gel matrices are used to detect conformational changes created by DNA sequence variation as alterations in electrophoretic mobility. Alternatively, where a polymorphism creates or destroys a recognition site for a restriction endonuclease, the sample is digested with that endonuclease, and the products size fractionated to determine whether the fragment was digested. Fractionation is performed by gel or capillary electrophoresis, particularly acrylamide or agarose gels.

Screening for mutations in a gene can be based on the functional or antigenic characteristics of the protein. Protein truncation assays are useful in detecting deletions that can affect the biological activity of the protein. Various immunoassays designed to detect polymorphisms in proteins can be used in screening. Where many diverse genetic mutations lead to a particular disease phenotype, functional protein assays have proven to be effective screening tools. The activity of the encoded protein can be determined by comparison with the wild-type protein.

Pattern matching in diagnosis using arrays. In another embodiment, the diagnostic and/or prognostic methods of the invention involve detection of expression of a selected set of genes in a test sample to produce a test expression pattern (TEP). The TEP is compared to a reference expression pattern (REP), which is generated by detection of expression of the selected set of genes in a reference sample (*e.g.*, a positive or negative control sample). The selected set of genes includes at least one of the genes of the invention, which genes correspond to the polynucleotide sequences of SEQ ID NOs:1-3351. Of particular interest is a selected set of genes that includes genes differentially expressed in the disease for which the test sample is to be screened.

"Reference sequences" or "reference polynucleotides" as used herein in the context of differential gene expression analysis and diagnosis/prognosis refers to a selected set of polynucleotides, which selected set includes at least one or more of the differentially expressed polynucleotides described herein. A plurality of reference sequences, preferably comprising positive and negative control sequences, can be included as reference sequences. Additional suitable reference sequences are found in Genbank, Unigene, and other nucleotide sequence databases (including, *e.g.*, expressed sequence tag (EST), partial, and full-length sequences).

"Reference array" means an array having reference sequences for use in hybridization with a sample, where the reference sequences include all, at least one of,

or any subset of the differentially expressed polynucleotides described herein. Usually such an array will include at least 3 different reference sequences, and can include any one or all of the provided differentially expressed sequences. Arrays of interest can further comprise sequences, including polymorphisms, of other genetic sequences, particularly other sequences of interest for screening for a disease or disorder (*e.g.*, cancer, dysplasia, or other related or unrelated diseases, disorders, or conditions). The oligonucleotide sequence on the array will usually be at least about 12 nt in length, and can be of about the length of the provided sequences, or can extend into the flanking regions to generate fragments of 100 nt to 200 nt in length or more. Reference arrays can be produced according to any suitable methods known in the art. For example, methods of producing large arrays of oligonucleotides are described in U.S. Patent NOs. 5,134,854 and 5,445,934 using light-directed synthesis techniques. Using a computer controlled system, a heterogeneous array of monomers is converted, through simultaneous coupling at a number of reaction sites, into a heterogeneous array of polymers. Alternatively, microarrays are generated by deposition of pre-synthesized oligonucleotides onto a solid substrate, for example as described in PCT published application no. WO 95/35505.

A "reference expression pattern" or "REP" as used herein refers to the relative levels of expression of a selected set of genes, particularly of differentially expressed genes, that is associated with a selected cell type, *e.g.*, a normal cell, a cancerous cell, a cell exposed to an environmental stimulus, and the like. A "test expression pattern" or "TEP" refers to relative levels of expression of a selected set of genes, particularly of differentially expressed genes, in a test sample (*e.g.*, a cell of unknown or suspected disease state, from which mRNA is isolated).

REPs can be generated in a variety of ways according to methods well known in the art. For example, REPs can be generated by hybridizing a control sample to an array having a selected set of polynucleotides (particularly a selected set of differentially expressed polynucleotides), acquiring the hybridization data from the array, and storing the data in a format that allows for ready comparison of the REP with a TEP. Alternatively, all expressed sequences in a control sample can be isolated and sequenced, *e.g.*, by isolating mRNA from a control sample, converting the mRNA into cDNA, and sequencing the cDNA. The resulting sequence information roughly or precisely reflects the identity and relative number of expressed sequences in the sample. The sequence information can then be stored in a format (*e.g.*, a computer-readable format) that allows for ready comparison of the REP with a TEP. The REP can be

normalized prior to or after data storage, and/or can be processed to selectively remove sequences of expressed genes that are of less interest or that might complicate analysis (*e.g.*, some or all of the sequences associated with housekeeping genes can be eliminated from REP data).

TEPs can be generated in a manner similar to REPs, *e.g.*, by hybridizing a test sample to an array having a selected set of polynucleotides, particularly a selected set of differentially expressed polynucleotides, acquiring the hybridization data from the array, and storing the data in a format that allows for ready comparison of the TEP with a REP. The REP and TEP to be used in a comparison can be generated simultaneously, or the TEP can be compared to previously generated and stored REPs.

In one embodiment of the invention, comparison of a TEP with a REP involves hybridizing a test sample with a reference array, where the reference array has one or more reference sequences for use in hybridization with a sample. The reference sequences include all, at least one of, or any subset of the differentially expressed polynucleotides described herein. Hybridization data for the test sample is acquired, the data normalized, and the produced TEP compared with a REP generated using an array having the same or similar selected set of differentially expressed polynucleotides. Probes that correspond to sequences differentially expressed between the two samples will show decreased or increased hybridization efficiency for one of the samples relative to the other.

Methods for collection of data from hybridization of samples with a reference arrays are well known in the art. For example, the polynucleotides of the reference and test samples can be generated using a detectable fluorescent label, and hybridization of the polynucleotides in the samples detected by scanning the microarrays for the presence of the detectable label using, for example, a microscope and light source for directing light at a substrate. A photon counter detects fluorescence from the substrate, while an x-y translation stage varies the location of the substrate. A confocal detection device that can be used in the subject methods is described in U.S. Patent No. 5,631,734. A scanning laser microscope is described in Shalon et al., *Genome Res.* (1996) *6*:639. A scan, using the appropriate excitation line, is performed for each fluorophore used. The digital images generated from the scan are then combined for subsequent analysis. For any particular array element, the ratio of the fluorescent signal from one sample (*e.g.*, a test sample) is compared to the fluorescent signal from another sample (*e.g.*, a reference sample), and the relative signal intensity determined.

Methods for analyzing the data collected from hybridization to arrays are well known in the art. For example, where detection of hybridization involves a fluorescent label, data analysis can include the steps of determining fluorescent intensity as a function of substrate position from the data collected, removing outliers, *i.e.*, data deviating from a predetermined statistical distribution, and calculating the relative binding affinity of the targets from the remaining data. The resulting data can be displayed as an image with the intensity in each region varying according to the binding affinity between targets and probes.

In general, the test sample is classified as having a gene expression profile corresponding to that associated with a disease or non-disease state by comparing the TEP generated from the test sample to one or more REPs generated from reference samples (*e.g.*, from samples associated with cancer or specific stages of cancer, dysplasia, samples affected by a disease other than cancer, normal samples, *etc.*). The criteria for a match or a substantial match between a TEP and a REP include expression of the same or substantially the same set of reference genes, as well as expression of these reference genes at substantially the same levels (*e.g.*, no significant difference between the samples for a signal associated with a selected reference sequence after normalization of the samples, or at least no greater than about 25% to about 40% difference in signal strength for a given reference sequence. In general, a pattern match between a TEP and a REP includes a match in expression, preferably a match in qualitative or quantitative expression level, of at least one of, all or any subset of the differentially expressed genes of the invention.

Pattern matching can be performed manually, or can be performed using a computer program. Methods for preparation of substrate matrices (*e.g.*, arrays), design of oligonucleotides for use with such matrices, labeling of probes, hybridization conditions, scanning of hybridized matrices, and analysis of patterns generated, including comparison analysis, are described in, for example, U.S. Patent No. 5,800,992.

<u>Diagnosis, Prognosis and Management of Cancer</u>

The polynucleotides of the invention and their gene products are of particular interest as genetic or biochemical markers (*e.g.*, in blood or tissues) that will detect the earliest changes along the carcinogenesis pathway and/or to monitor the efficacy of various therapies and preventive interventions. For example, the level of expression of certain polynucleotides can be indicative of a poorer prognosis, and

therefore warrant more aggressive chemo- or radio-therapy for a patient or vice versa. The correlation of novel surrogate tumor specific features with response to treatment and outcome in patients can define prognostic indicators that allow the design of tailored therapy based on the molecular profile of the tumor. These therapies include antibody targeting and gene therapy. Determining expression of certain polynucleotides and comparison of a patients profile with known expression in normal tissue and variants of the disease allows a determination of the best possible treatment for a patient, both in terms of specificity of treatment and in terms of comfort level of the patient. Surrogate tumor markers, such as polynucleotide expression, can also be used to better classify, and thus diagnose and treat, different forms and disease states of cancer. Two classifications widely used in oncology that can benefit from identification of the expression levels of the polynucleotides of the invention are staging of the cancerous disorder, and grading the nature of the cancerous tissue.

The polynucleotides of the invention can be useful to monitor patients having or susceptible to cancer to detect potentially malignant events at a molecular level before they are detectable at a gross morphological level. Furthermore, a polynucleotide of the invention identified as important for one type of cancer can also have implications for development or risk of development of other types of cancer, *e.g.*, where a polynucleotide is differentially expressed across various cancer types. Thus, for example, expression of a polynucleotide that has clinical implications for metastatic colon cancer can also have clinical implications for stomach cancer or endometrial cancer.

Staging. Staging is a process used by physicians to describe how advanced the cancerous state is in a patient. Generally, if a cancer is only detectable in the area of the primary lesion without having spread to any lymph nodes it is called Stage I. If it has spread only to the closest lymph nodes, it is called Stage II. In Stage III, the cancer has generally spread to the lymph nodes in near proximity to the site of the primary lesion. Cancers that have spread to a distant part of the body, such as the liver, bone, brain or other site, are Stage IV, the most advanced stage.

The polynucleotides of the invention can facilitate fine-tuning of the staging process by identifying markers for the aggresivity of a cancer, *e.g.*, the metastatic potential, as well as the presence in different areas of the body. Thus, a Stage II cancer with a polynucleotide signifying a high metastatic potential cancer can be used to change a borderline Stage II tumor to a Stage III tumor, justifying more aggressive

therapy. Conversely, the presence of a polynucleotide signifying a lower metastatic potential allows more conservative staging of a tumor.

Grading of cancers. Grade is a term used to describe how closely a tumor resembles normal tissue of its same type. The microscopic appearance of a tumor is used to identify tumor grade based on parameters such as cell morphology, cellular organization, and other markers of differentiation. As a general rule, the grade of a tumor corresponds to its rate of growth or aggressiveness, with undifferentiated or high-grade tumors being more aggressive than well differentiated or low-grade tumors. The following guidelines are generally used for grading tumors: 1) GX Grade cannot be assessed; 2) G1 Well differentiated; G2 Moderately well differentiated; 3) G3 Poorly differentiated; 4) G4 Undifferentiated. The polynucleotides of the invention can be especially valuable in determining the grade of the tumor, as they not only can aid in determining the differentiation status of the cells of a tumor, they can also identify factors other than differentiation that are valuable in determining the aggressivity of a tumor, such as metastatic potential.

Detection of lung cancer. The polynucleotides of the invention can be used to detect lung cancer in a subject. Although there are more than a dozen different kinds of lung cancer, the two main types of lung cancer are small cell and nonsmall cell, which encompass about 90% of all lung cancer cases. Small cell carcinoma (also called oat cell carcinoma) usually starts in one of the larger bronchial tubes, grows fairly rapidly, and is likely to be large by the time of diagnosis. Nonsmall cell lung cancer (NSCLC) is made up of three general subtypes of lung cancer. Epidermoid carcinoma (also called squamous cell carcinoma) usually starts in one of the larger bronchial tubes and grows relatively slowly. The size of these tumors can range from very small to quite large. Adenocarcinoma starts growing near the outside surface of the lung and can vary in both size and growth rate. Some slowly growing adenocarcinomas are described as alveolar cell cancer. Large cell carcinoma starts near the surface of the lung, grows rapidly, and the growth is usually fairly large when diagnosed. Other less common forms of lung cancer are carcinoid, cylindroma, mucoepidermoid, and malignant mesothelioma.

The polynucleotides of the invention, *e.g.*, polynucleotides differentially expressed in normal cells versus cancerous lung cells (*e.g.*, tumor cells of high or low metastatic potential) or between types of cancerous lung cells (*e.g.*, high metastatic versus low metastatic), can be used to distinguish types of lung cancer as well as identifying traits specific to a certain patient's cancer and selecting an appropriate

therapy. For example, if the patient's biopsy expresses a polynucleotide that is associated with a low metastatic potential, it may justify leaving a larger portion of the patient's lung in surgery to remove the lesion. Alternatively, a smaller lesion with expression of a polynucleotide that is associated with high metastatic potential may justify a more radical removal of lung tissue and/or the surrounding lymph nodes, even if no metastasis can be identified through pathological examination.

Detection of breast cancer. The majority of breast cancers are adenocarcinomas subtypes, which can be summarized as follows: 1) ductal carcinoma *in situ* (DCIS), including comedocarcinoma; 2) infiltrating (or invasive) ductal carcinoma (IDC); 3) lobular carcinoma *in situ* (LCIS); 4) infiltrating (or invasive) lobular carcinoma (ILC); 5) inflammatory breast cancer; 6) medullary carcinoma; 7) mucinous carcinoma; 8) Paget's disease of the nipple; 9) Phyllodes tumor; and 10) tubular carcinoma.

The expression of polynucleotides of the invention can be used in the diagnosis and management of breast cancer, as well as to distinguish between types of breast cancer. Detection of breast cancer can be determined using expression levels of any of the appropriate polynucleotides of the invention, either alone or in combination. Determination of the aggressive nature and/or the metastatic potential of a breast cancer can also be determined by comparing levels of one or more polynucleotides of the invention and comparing levels of another sequence known to vary in cancerous tissue, *e.g.*, ER expression. In addition, development of breast cancer can be detected by examining the ratio of expression of a differentially expressed polynucleotide to the levels of steroid hormones (*e.g.*, testosterone or estrogen) or to other hormones (*e.g.*, growth hormone, insulin). Thus expression of specific marker polynucleotides can be used to discriminate between normal and cancerous breast tissue, to discriminate between breast cancers with different cells of origin, to discriminate between breast cancers with different potential metastatic rates, *etc*.

Detection of colon cancer. The polynucleotides of the invention exhibiting the appropriate expression pattern can be used to detect colon cancer in a subject. Colorectal cancer is one of the most common neoplasms in humans and perhaps the most frequent form of hereditary neoplasia. Prevention and early detection are key factors in controlling and curing colorectal cancer. Colorectal cancer begins as polyps, which are small, benign growths of cells that form on the inner lining of the colon. Over a period of several years, some of these polyps accumulate additional mutations and become cancerous. Multiple familial colorectal cancer disorders have

been identified, which are summarized as follows: 1) Familial adenomatous polyposis (FAP); 2) Gardner's syndrome; 3) Hereditary nonpolyposis colon cancer (HNPCC); and 4) Familial colorectal cancer in Ashkenazi Jews. The expression of appropriate polynucleotides of the invention can be used in the diagnosis, prognosis and management of colorectal cancer. Detection of colon cancer can be determined using expression levels of any of these sequences alone or in combination with the levels of expression. Determination of the aggressive nature and/or the metastatic potential of a colon cancer can be determined by comparing levels of one or more polynucleotides of the invention and comparing total levels of another sequence known to vary in cancerous tissue, *e.g.*, expression of p53, DCC ras, lor FAP (see, *e.g.*, Fearon ER, et al., *Cell* (1990) *61*(*5*):759; Hamilton SR et al., *Cancer* (1993) *72*:957; Bodmer W, et al., *Nat Genet.* (1994) *4*(*3*):217; Fearon ER, *Ann N Y Acad Sci.* (1995) *768*:101). For example, development of colon cancer can be detected by examining the ratio of any of the polynucleotides of the invention to the levels of oncogenes (*e.g.*, ras) or tumor suppressor genes (*e.g.*, FAP or p53). Thus expression of specific marker polynucleotides can be used to discriminate between normal and cancerous colon tissue, to discriminate between colon cancers with different cells of origin, to discriminate between colon cancers with different potential metastatic rates, *etc*.

Use of Polynucleotides to Screen for Peptide Analogs and Antagonists

Polypeptides encoded by the instant polynucleotides and corresponding full length genes can be used to screen peptide libraries to identify binding partners, such as receptors, from among the encoded polypeptides. Peptide libraries can be synthesized according to methods known in the art (see, *e.g.*, U.S. Patent No. 5,010,175, and WO 91/17823). Agonists or antagonists of the polypeptides if the invention can be screened using any available method known in the art, such as signal transduction, antibody binding, receptor binding, mitogenic assays, chemotaxis assays, *etc*. The assay conditions ideally should resemble the conditions under which the native activity is exhibited *in vivo*, that is, under physiologic pH, temperature, and ionic strength. Suitable agonists or antagonists will exhibit strong inhibition or enhancement of the native activity at concentrations that do not cause toxic side effects in the subject. Agonists or antagonists that compete for binding to the native polypeptide can require concentrations equal to or greater than the native concentration, while inhibitors capable of binding irreversibly to the polypeptide can be added in concentrations on the order of the native concentration.

Such screening and experimentation can lead to identification of a novel polypeptide binding partner, such as a receptor, encoded by a gene or a cDNA corresponding to a polynucleotide of the invention, and at least one peptide agonist or antagonist of the novel binding partner. Such agonists and antagonists can be used to modulate, enhance, or inhibit receptor function in cells to which the receptor is native, or in cells that possess the receptor as a result of genetic engineering. Further, if the novel receptor shares biologically important characteristics with a known receptor, information about agonist/antagonist binding can facilitate development of improved agonists/antagonists of the known receptor.

Pharmaceutical Compositions and Therapeutic Uses

Pharmaceutical compositions of the invention can comprise polypeptides, antibodies, or polynucleotides (including antisense nucleotides and ribozymes) of the claimed invention in a therapeutically effective amount. The term "therapeutically effective amount" as used herein refers to an amount of a therapeutic agent to treat, ameliorate, or prevent a desired disease or condition, or to exhibit a detectable therapeutic or preventative effect. The effect can be detected by, for example, chemical markers or antigen levels. Therapeutic effects also include reduction in physical symptoms, such as decreased body temperature. The precise effective amount for a subject will depend upon the subject's size and health, the nature and extent of the condition, and the therapeutics or combination of therapeutics selected for administration. Thus, it is not useful to specify an exact effective amount in advance. However, the effective amount for a given situation is determined by routine experimentation and is within the judgment of the clinician. For purposes of the present invention, an effective dose will generally be from about 0.01 mg/ kg to 50 mg/kg or 0.05 mg/kg to about 10 mg/kg of the DNA constructs in the individual to which it is administered.

A pharmaceutical composition can also contain a pharmaceutically acceptable carrier. The term "pharmaceutically acceptable carrier" refers to a carrier for administration of a therapeutic agent, such as antibodies or a polypeptide, genes, and other therapeutic agents. The term refers to any pharmaceutical carrier that does not itself induce the production of antibodies harmful to the individual receiving the composition, and which can be administered without undue toxicity. Suitable carriers can be large, slowly metabolized macromolecules such as proteins, polysaccharides, polylactic acids, polyglycolic acids, polymeric amino acids, amino acid copolymers,

and inactive virus particles. Such carriers are well known to those of ordinary skill in the art. Pharmaceutically acceptable carriers in therapeutic compositions can include liquids such as water, saline, glycerol and ethanol. Auxiliary substances, such as wetting or emulsifying agents, pH buffering substances, and the like, can also be present in such vehicles. Typically, the therapeutic compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid vehicles prior to injection can also be prepared. Liposomes are included within the definition of a pharmaceutically acceptable carrier. Pharmaceutically acceptable salts can also be present in the pharmaceutical composition, *e.g.*, mineral acid salts such as hydrochlorides, hydrobromides, phosphates, sulfates, and the like; and the salts of organic acids such as acetates, propionates, malonates, benzoates, and the like. A thorough discussion of pharmaceutically acceptable excipients is available in *Remington's Pharmaceutical Sciences* (Mack Pub. Co., New Jersey, 1991).

Delivery Methods. Once formulated, the compositions of the invention can be (1) administered directly to the subject (*e.g.*, as polynucleotide or polypeptides); or (2) delivered *ex vivo*, to cells derived from the subject (*e.g.*, as in *ex vivo* gene therapy). Direct delivery of the compositions will generally be accomplished by parenteral injection, *e.g.*, subcutaneously, intraperitoneally, intravenously or intramuscularly, intratumoral or to the interstitial space of a tissue. Other modes of administration include oral and pulmonary administration, suppositories, and transdermal applications, needles, and gene guns or hyposprays. Dosage treatment can be a single dose schedule or a multiple dose schedule.

Methods for the *ex vivo* delivery and reimplantation of transformed cells into a subject are known in the art and described in *e.g.*, International Publication No. WO 93/14778. Examples of cells useful in *ex vivo* applications include, for example, stem cells, particularly hematopoetic, lymph cells, macrophages, dendritic cells, or tumor cells. Generally, delivery of nucleic acids for both *ex vivo* and *in vitro* applications can be accomplished by, for example, dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei, all well known in the art.

Once a gene corresponding to a polynucleotide of the invention has been found to correlate with a proliferative disorder, such as neoplasia, dysplasia, and hyperplasia, the disorder can be amenable to treatment by administration of a

therapeutic agent based on the provided polynucleotide, corresponding polypeptide or other corresponding molecule (*e.g.*, antisense, ribozyme, *etc.*).

The dose and the means of administration of the inventive pharmaceutical compositions are determined based on the specific qualities of the therapeutic composition, the condition, age, and weight of the patient, the progression of the disease, and other relevant factors. For example, administration of polynucleotide therapeutic compositions agents of the invention includes local or systemic administration, including injection, oral administration, particle gun or catheterized administration, and topical administration. Preferably, the therapeutic polynucleotide composition contains an expression construct comprising a promoter operably linked to a polynucleotide of at least 12, 22, 25, 30, or 35 contiguous nt of the polynucleotide disclosed herein. Various methods can be used to administer the therapeutic composition directly to a specific site in the body. For example, a small metastatic lesion is located and the therapeutic composition injected several times in several different locations within the body of tumor. Alternatively, arteries which serve a tumor are identified, and the therapeutic composition injected into such an artery, in order to deliver the composition directly into the tumor. A tumor that has a necrotic center is aspirated and the composition injected directly into the now empty center of the tumor. The antisense composition is directly administered to the surface of the tumor, for example, by topical application of the composition. X-ray imaging is used to assist in certain of the above delivery methods.

Receptor-mediated targeted delivery of therapeutic compositions containing an antisense polynucleotide, subgenomic polynucleotides, or antibodies to specific tissues can also be used. Receptor-mediated DNA delivery techniques are described in, for example, Findeis et al., *Trends Biotechnol.* (1993) *11*:202; Chiou et al., *Gene Therapeutics: Methods And Applications Of Direct Gene Transfer* (J.A. Wolff, ed.) (1994); Wu et al., *J. Biol. Chem.* (1988) *263*:621; Wu et al., *J. Biol. Chem.* (1994) *269*:542; Zenke et al., *Proc. Natl. Acad. Sci.* (USA) (1990) *87*:3655; Wu et al., *J. Biol. Chem.* (1991) *266*:338. Therapeutic compositions containing a polynucleotide are administered in a range of about 100 ng to about 200 mg of DNA for local administration in a gene therapy protocol. Concentration ranges of about 500 ng to about 50 mg, about 1 mg to about 2 mg, about 5 mg to about 500 mg, and about 20 mg to about 100 mg of DNA can also be used during a gene therapy protocol. Factors such as method of action (*e.g.*, for enhancing or inhibiting levels of the encoded gene product) and efficacy of transformation and expression are considerations which will

affect the dosage required for ultimate efficacy of the antisense subgenomic polynucleotides. Where greater expression is desired over a larger area of tissue, larger amounts of antisense subgenomic polynucleotides or the same amounts readministered in a successive protocol of administrations, or several administrations to different adjacent or close tissue portions of, for example, a tumor site, may be required to effect a positive therapeutic outcome. In all cases, routine experimentation in clinical trials will determine specific ranges for optimal therapeutic effect. For polynucleotide-related genes encoding polypeptides or proteins with anti-inflammatory activity, suitable use, doses, and administration are described in U.S. Patent No. 5,654,173.

The therapeutic polynucleotides and polypeptides of the present invention can be delivered using gene delivery vehicles. The gene delivery vehicle can be of viral or non-viral origin (see generally, Jolly, *Cancer Gene Therapy* (1994) *1*:51; Kimura, *Human Gene Therapy* (1994) *5*:845; Connelly, *Human Gene Therapy* (1995) *1*:185; and Kaplitt, *Nature Genetics* (1994) 6:148). Expression of such coding sequences can be induced using endogenous mammalian or heterologous promoters. Expression of the coding sequence can be either constitutive or regulated.

Viral-based vectors for delivery of a desired polynucleotide and expression in a desired cell are well known in the art. Exemplary viral-based vehicles include, but are not limited to, recombinant retroviruses (see, *e.g.*, WO 90/07936; WO 94/03622; WO 93/25698; WO 93/25234; U.S. Patent No. 5, 219,740; WO 93/11230; WO 93/10218; U.S. Patent No. 4,777,127; GB Patent No. 2,200,651; EP 0 345 242; and WO 91/02805), alphavirus-based vectors (*e.g.*, Sindbis virus vectors, Semliki forest virus (ATCC VR-67; ATCC VR-1247), Ross River virus (ATCC VR-373; ATCC VR-1246) and Venezuelan equine encephalitis virus (ATCC VR-923; ATCC VR-1250; ATCC VR 1249; ATCC VR-532), and adeno-associated virus (AAV) vectors (see, *e.g.*, WO 94/12649, WO 93/03769; WO 93/19191; WO 94/28938; WO 95/11984 and WO 95/00655). Administration of DNA linked to killed adenovirus as described in Curiel, *Hum. Gene Ther.* (1992) *3*:147 can also be employed.

Non-viral delivery vehicles and methods can also be employed, including, but not limited to, polycationic condensed DNA linked or unlinked to killed adenovirus alone (see, *e.g.*, Curiel, *Hum. Gene Ther.* (1992) *3*:147); ligand-linked DNA(see, *e.g.*, Wu, *J. Biol. Chem.* *264*:16985 (1989)); eukaryotic cell delivery vehicles cells (see, *e.g.*, U.S. Patent No. 5,814,482; WO 95/07994; WO 96/17072; WO 95/30763; and WO 97/42338) and nucleic charge neutralization or fusion with cell membranes. Naked DNA can also be employed. Exemplary naked DNA introduction

methods are described in WO 90/11092 and U.S. Patent No. 5,580,859. Liposomes that can act as gene delivery vehicles are described in U.S. Patent No. 5,422,120; WO 95/13796; WO 94/23697; WO 91/14445; and EP 0524968. Additional approaches are described in Philip, *Mol. Cell Biol. 14*:2411 (1994), and in Woffendin, *Proc. Natl. Acad. Sci.* (1994) *91*:1581.

Further non-viral delivery suitable for use includes mechanical delivery systems such as the approach described in Woffendin et al., *Proc. Natl. Acad. Sci. USA 91*(24):11581 (1994). Moreover, the coding sequence and the product of expression of such can be delivered through deposition of photopolymerized hydrogel materials or use of ionizing radiation (see, *e.g.*, U.S. Patent No. 5,206,152 and WO 92/11033). Other conventional methods for gene delivery that can be used for delivery of the coding sequence include, for example, use of hand-held gene transfer particle gun (see, *e.g.*, U.S. Patent No. 5,149,655); use of ionizing radiation for activating transferred gene (see, *e.g.*, U.S. Patent No. 5,206,152 and WO 92/11033).

The present invention will now be illustrated by reference to the following examples which set forth particularly advantageous embodiments. However, it should be noted that these embodiments are illustrative and are not to be construed as restricting the invention in any way.

EXAMPLES

EXAMPLE 1

Source of Biological Materials and Overview of Novel Polynucleotides Expressed by the Biological Materials

Cell lines and human normal and tumor tissue were used to construct cDNA libraries from mRNA isolated from the cells and tissues. Most sequences were about 275-300 nucleotides in length. The cells lines include Km12L4-A cell line, a high metastatic colon cancer cell line (Morika, W. A. K. et al., *Cancer Research* (1988) *48*:6863). The KM12L4-A cell line is derived from the KM12C cell line. The KM12C cell line, which is poorly metastatic (low metastatic) was established in culture from a Dukes' stage B2 surgical specimen (Morikawa et al. *Cancer Res.* (1988) *48*:6863). The KML4-A is a highly metastatic subline derived from KM12C (Yeatman et al. *Nucl. Acids. Res.* (1995) *23*:4007; Bao-Ling et al. *Proc. Annu. Meet. Am. Assoc. Cancer. Res.* (1995) *21*:3269). The KM12C and KM12C-derived cell lines (*e.g.*, KM12L4, KM12L4-A, *etc.*) are well-recognized in the art as model cell lines for the study of colon cancer (see, *e.g.*, Moriakawa et al., *supra*; Radinsky et al. *Clin. Cancer Res.* (1995) 1:19; Yeatman et al., (1995) *supra*; Yeatman et al., *Clin. Exp. Metastasis* (1996) 14:246). These and other cell lines and tissue are described in Table 6.

The sequences of the isolated polynucleotides were first masked to eliminate low complexity sequences using the XBLAST masking program (Claverie "Effective Large-Scale Sequence Similarity Searches," In: Computer Methods for Macromolecular Sequence Analysis, Doolittle, ed., *Meth. Enzymol. 266*:212-227 Academic Press, NY, NY (1996); see particularly Claverie, in "Automated DNA Sequencing and Analysis Techniques" Adams et al., eds., Chap. 36, p. 267 Academic Press, San Diego, 1994 and Claverie et al. *Comput. Chem.* (1993) *17*:191). Generally, masking does not influence the final search results, except to eliminate sequences of relative little interest due to their low complexity, and to eliminate multiple "hits" based on similarity to repetitive regions common to multiple sequences, *e.g.*, Alu repeats. The sequences remaining after masking were then used in a BLASTN vs. Genbank search; sequences that exhibited greater than 70% overlap, 99% identity, and a p value of less than 1×10^{-40} were discarded. Sequences from this search also were discarded if the inclusive parameters were met, but the sequence was ribosomal or vector-derived.

The resulting sequences from the previous search were classified into three groups (1, 2 and 3 below) and searched in a BLASTX vs. NRP (non-redundant proteins) database search: (1) unknown (no hits in the Genbank search), (2) weak similarity (greater than 45% identity and p value of less than 1 x 10^{-5}), and (3) high similarity (greater than 60% overlap, greater than 80% identity, and p value less than 1 x 10^{-5}). Sequences having greater than 70% overlap, greater than 99% identity, and p value of less than 1 x 10^{-40} were discarded.

The remaining sequences were classified as unknown (no hits), weak similarity, and high similarity (parameters as above). Two searches were performed on these sequences. First, a BLAST vs. EST database search was performed and sequences with greater than 99% overlap, greater than 99% similarity and a p value of less than 1 x 10^{-40} were discarded. Sequences with a p value of less than 1 x 10^{-65} when compared to a database sequence of human origin were also excluded. Second, a BLASTN vs. Patent GeneSeq database was performed and sequences having greater than 99% identity, p value less than 1 x 10^{-40}, and greater than 99% overlap were discarded.

The remaining sequences were subjected to screening using other rules and redundancies in the dataset. Sequences with a p value of less than 1 x 10^{-111} in relation to a database sequence of human origin were specifically excluded. The final result provided the 3351 sequences listed in the accompanying Sequence Listing. Each identified polynucleotide represents sequence from at least a partial mRNA transcript. Polynucleotides that were determined to be novel were assigned a sequence identification number.

The novel polynucleotides were assigned sequence identification numbers SEQ ID NOs:1-3351. The first 1847 DNA sequences corresponding to the novel polynucleotides are provided in the Sequence Listing in Table 1. DNA sequences corresponding to the novel polynucleotides of SEQ ID NOs:1848-3351 are provided in the Sequence Listing in Table 2. The DNA sequences of Table 2, while numbered SEQ ID 1-1504, correspond to SEQ ID NOs:1848-3351 in the Sequence Listing, *e.g.*, Table 2 SEQ ID 1 is SEQ ID NO:1848, Table 2 SEQ ID 2 is SEQ ID NO:1849, *etc.* Each DNA sequence in Table 4 is uniquely identified by a number that is 1847 less than its SEQ ID NO in the Sequence Listing. Tables 1 and 2 provide: 1) the SEQ ID NO assigned to each sequence for use in the present specification or a corresponding number; 2) the sequence name used as an internal identifier of the sequence; 3) the name assigned to the clone from which the

sequence was isolated; and 4) the number of the cluster to which the sequence is assigned (Cluster ID; where the cluster ID is 0, the sequence was not assigned to any cluster).

Because the provided polynucleotides represent partial mRNA transcripts, two or more polynucleotides of the invention may represent different regions of the same mRNA transcript and the same gene. Thus, if two or more SEQ ID NOs: are identified as belonging to the same clone, then either sequence can be used to obtain the full-length mRNA or gene.

EXAMPLE 2

RESULTS OF PUBLIC DATABASE SEARCH TO IDENTIFY FUNCTION OF GENE PRODUCTS

SEQ ID NOs:1-3351 were translated in all three reading frames to determine the best alignment with the individual sequences. These amino acid sequences and nucleotide sequences are referred to, generally, as query sequences, which are aligned with the individual sequences. Query and individual sequences were aligned using the BLAST programs, available over the world wide web at http://www.ncbi.nlm.nih.gov/BLAST/. Again the sequences were masked to various extents to prevent searching of repetitive sequences or poly-A sequences, using the XBLAST program for masking low complexity as described above in Example 1.

Tables 3 and 4 (inserted before the claims) show the results of the alignments. Table 3 contains alignment information for SEQ ID NOs:1-1847 and Table 4 contains alignment information for SEQ ID NOs:1848-3351. The DNA sequences of Table 4, while numbered SEQ ID 1-1504, correspond to SEQ ID NOs:1848-3351. Each DNA sequence in Table 4 is uniquely identified by a number that is 1847 less than its SEQ ID NO. Tables 3 and 4 refer to each sequence by its SEQ ID NO or a corresponding number, the accession numbers and descriptions of nearest neighbors from the Genbank and Non-Redundant Protein searches, and the p values of the search results.

For each of SEQ ID NOs:1-1847, the best alignment to a protein or DNA sequence is included in Table 3, and the best alignment for each of SEQ ID NOs:1848-3351 is included in Table 4. The activity of the polypeptide encoded by SEQ ID NOs:1-3351 is the same or similar to the nearest neighbor reported in Table 3 or 4. The accession number of the nearest neighbor is reported, providing a reference to the activities exhibited by the nearest neighbor. The search program and database used for the alignment also are indicated as well as a calculation of the p value.

Full length sequences or fragments of the polynucleotide sequences of the nearest neighbors can be used as probes and primers to identify and isolate the full length sequence of SEQ ID NOs:1-3351. The nearest neighbors can indicate a tissue or cell type to be used to construct a library for the full-length sequences of SEQ ID NOs:1-3351.

EXAMPLE 3

MEMBERS OF PROTEIN FAMILIES

The sequences (SEQ ID NOs:1-3351) were used to conduct a profile search as described in the specification above. Several of the polynucleotides of the invention were found to encode polypeptides having characteristics of a polypeptide belonging to a known protein families (and thus represent new members of these protein families) and/or comprising a known functional domain (Table 5). "Start" and "stop" in Table 3 indicate the position within the individual sequences that align with the query sequence having the indicated SEQ ID NO. The direction indicates the orientation of the query sequence with respect to the individual sequence, where forward (for) indicates that the alignment is in the same direction (left to right) as the sequence provided in the Sequence Listing and reverse (rev) indicates that the alignment is with a sequence complementary to the sequence provided in the Sequence Listing.

Some polynucleotides exhibited multiple profile hits because, for example, the particular sequence contains overlapping profile regions, and/or the sequence contains two different functional domains. These profile hits are described in more detail below.

<u>Ank Repeats (ANK)</u>. SEQ ID NOs:187, 1268, 1804, 1819, 1830, 1839, 2652, 3015 and 3267 represent polynucleotides encoding an Ank repeat-containing protein. The ankyrin motif is a 33 amino acid sequence named for the protein ankyrin which has 24 tandem 33-amino-acid motifs. Ank repeats were originally identified in the cell-cycle-control protein cdc10 (Breeden et al., *Nature* (1987) *329*:651). Proteins containing ankyrin repeats include ankyrin, myotropin, I-kappaB proteins, cell cycle protein cdc10, the Notch receptor (Matsuno et al., *Development* (1997) *124*(*21*):4265); G9a (or BAT8) of the class III region of the major histocompatibility complex (*Biochem J.* *290*:811-818, 1993), FABP, GABP, 53BP2, Lin12, glp-1, SW14, and SW16. The functions of the ankyrin repeats are compatible with a role in protein-

protein interactions (Bork, *Proteins* (1993) *17(4)*:363; Lambert and Bennet, *Eur. J. Biochem.* (1993) *211*:1; Kerr et al., *Current Op. Cell Biol.* (1992) *4*:496; Bennet et al., *J. Biol. Chem.* (1980) *255*:6424).

ATPases Associated with Various Cellular Activities (ATPases). Sequences within SEQ ID NOs:431, 639, 2135, 2684, 2859, 3197 and 3266 correspond to a sequence that encodes a novel member of the "ATPases Associated with diverse cellular Activities" (AAA) protein family. The AAA protein family is composed of a large number of ATPases that share a conserved region of about 220 amino acids that contains an ATP-binding site (Froehlich et al., *J. Cell Biol.* (1991) *114*:443; Erdmann et al., *Cell* (1991) *64*:499; Peters et al., *EMBO J.* (1990) *9*:1757; Kunau et al., *Biochimie* (1993) *75*:209-224; Confalonieri et al., *BioEssays* (1995) *17*:639; http://yeamob.pci.chemie.uni-tuebingen.de/AAA/Description.html). The proteins that belong to this family either contain one or two AAA domains. In general, the AAA domains in these proteins act as ATP-dependent protein clamps (Confalonieri et al. (1995) *BioEssays 17*:639). In addition to the ATP-binding 'A' and 'B' motifs, which are located in the N-terminal half of this domain, there is a highly conserved region located in the central part of the domain which was used in the development of the signature pattern. The consensus pattern is: [LIVMT]-x-[LIVMT]-[LIVMF]-x-[GATMC]-[ST]-[NS]-x(4)-[LIVM]- D-x-A-[LIFA]-x-R.

Bromodomain (bromodomain). SEQ ID NO:1814 represents a polynucleotide encoding a polypeptide having a bromodomain region (Haynes et al., 1992, Nucleic Acids Res. 20:2693-2603, Tamkun et al., 1992, Cell 68:561-572, and Tamkun, 1995, Curr. Opin. Genet. Dev. 5:473-477), which is a conserved region of about 70 amino acids. The bromodomain is thought to be involved in protein-protein interactions and may be important for the assembly or activity of multicomponent complexes involved in transcriptional activation. The consensus pattern, which spans a major part of the bromodomain, is: [STANVF]-x(2)-F-x(4)-[DNS]-x(5,7)-[DENQTF]-Y-[HFY]-x(2)- [LIVMFY]-x(3)-[LIVM]-x(4)-[LIVM]-x(6,8)-Y-x(12,13)-[LIVM]-x(2)-N-[SACF]-x(2)-[FY].

Basic Region Plus Leucine Zipper Transcription Factors (BZIP). SEQ ID NOs:410, 552, 768, 822, 836, 1288, 1365, 1454, 1540, 1549, 1556, 1557, 1563, 1622, 1630, 1704, 1808, 2363, 2424, 3147, 3152, 3158 and 3208 represent polynucleotides encoding a novel member of the family of basic region plus leucine zipper transcription factors. The bZIP superfamily (Hurst, *Protein Prof.* (1995) *2*:105; and Ellenberger, *Curr. Opin. Struct. Biol.* (1994) *4*:12) of eukaryotic DNA-binding

transcription factors encompasses proteins that contain a basic region mediating sequence-specific DNA-binding followed by a leucine zipper required for dimerization. The consensus pattern for this protein family is: [KR]-x(1,3)-[RKSAQ]-N-x(2)-[SAQ](2)-x-[RKTAENQ]-x-R-x-[RK].

<u>EF Hand (EFhand)</u>. SEQ ID NOs:820, 1755 and 3285 correspond to polynucleotides encoding a novel protein in the family of EF-hand proteins. Many calcium-binding proteins belong to the same evolutionary family and share a type of calcium-binding domain known as the EF-hand (Kawasaki et al., *Protein. Prof.* (1995) *2*:305-490). This type of domain consists of a twelve residue loop flanked on both sides by a twelve residue alpha-helical domain. In an EF-hand loop the calcium ion is coordinated in a pentagonal bipyramidal configuration. The six residues involved in the binding are in positions 1, 3, 5, 7, 9 and 12; these residues are denoted by X, Y, Z, -Y, -X and -Z. The invariant Glu or Asp at position 12 provides two oxygens for liganding Ca (bidentate ligand). The consensus pattern includes the complete EF-hand loop as well as the first residue which follows the loop and which seem to always be hydrophobic: D-x-[DNS]-{ILVFYW}-[DENSTG]-[DNQGHRK]-{GP}-[LIVMC]-[DENQSTAGC]-x(2)-[DE]-[LIVMFYW].

<u>Ets Domain (Ets Nterm)</u>. SEQ ID NO:1811 represents a polynucleotide encoding a polypeptide with N-terminal homology in ETS domain. Proteins of this family contain a conserved domain, the "ETS-domain," that is involved in DNA binding. The domain appears to recognize purine-rich sequences; it is about 85 to 90 amino acids in length, and is rich in aromatic and positively charged residues (Wasylyk, et al., *Eur. J. Biochem.* (1993) *211*:718). The *ets* gene family encodes a novel class of DNA-binding proteins, each of which binds a specific DNA sequence and comprises an *ets* domain that specifically interacts with sequences containing the common core tri-nucleotide sequence GGA. In addition to an *ets* domain, native *ets* proteins comprise other sequences which can modulate the biological specificity of the protein. *Ets* genes and proteins are involved in a variety of essential biological processes including cell growth, differentiation and development, and three members are implicated in oncogenic process.

<u>G-Protein Alpha Subunit (G-alpha)</u>. SEQ ID NO:1846 represents a polynucleotide encoding a novel polypeptide of the G-protein alpha subunit family. Guanine nucleotide binding proteins (G-proteins) are a family of membrane-associated proteins that couple extracellularly-activated integral-membrane receptors to intracellular effectors, such as ion channels and enzymes that vary the concentration of

second messenger molecules. G-proteins are composed of 3 subunits (alpha, beta and gamma) which, in the resting state, associate as a trimer at the inner face of the plasma membrane. The alpha subunit binds GTP and exhibits GTPase activity. G-protein alpha subunits are 350-400 amino acids in length and have molecular weights in the range 40-45 kDa. Seventeen distinct types of alpha subunit have been identified in mammals, and fall into 4 main groups on the basis of both sequence similarity and function: alpha-s, alpha-q, alpha-i and alpha-12 (Simon et al., *Science* (1993) *252*:802). They are often N-terminally acylated, usually with myristate and/or palmitoylate, and these fatty acid modifications can be important for membrane association and high- affinity interactions with other proteins.

Helicases conserved C-terminal domain (helicase_C). SEQ ID NOs:1496, 2826 and 2871 represent polynucleotides encoding novel members of the DEAD/H helicase family. A number of eukaryotic and prokaryotic proteins have been characterized (Schmid S.R., et al., *Mol. Microbiol.* (1992) *6*:283; Linder P., et al., *Nature* (1989) *337*:121; Wassarman D.A., et al., *Nature* (1991) *349*:463) on the basis of their structural similarity. All are involved in ATP-dependent, nucleic-acid unwinding. All DEAD box family members of the above proteins share a number of conserved sequence motifs, some of which are specific to the DEAD family while others are shared by other ATP-binding proteins or by proteins belonging to the helicases 'superfamily' (Hodgman T.C., *Nature* (1988) *333*:22 and *Nature* (1988) *333*:578 (Errata). One of these motifs, called the "D-E-A-D-box", represents a special version of the B motif of ATP-binding proteins. Some other proteins belong to a subfamily which have His instead of the second Asp and are thus said to be "D-E-A-H-box" proteins (Wassarman D.A., et al., *Nature* (1991) *349*:463; Harosh I., et al., *Nucleic Acids Res.* (1991) *19*:6331; Koonin E.V. et al., *J. Gen. Virol.* (1992) *73*:989. The following signature patterns are used to identify members of both subfamilies: 1) [LIVMF](2)-D-E-A-D-[RKEN]-x-[LIVMFYGSTN]; and 2) [GSAH]-x-[LIVMF](3)-D-E-[ALIV]-H-[NECR].

Homeobox domain (homeobox). SEQ ID NOs:1676, 1820 and 1821 represent polynucleotides encoding proteins having a homeobox domain. The homeobox is a protein domain of 60 amino acids (Gehring In: Guidebook to the Homeobox Genes, Duboule D., Ed., pp. 1-10, Oxford University Press, Oxford, (1994); Buerglin In: Guidebook to the Homeobox Genes, pp25-72, Oxford University Press, Oxford, (1994); Gehring, *Trends Biochem. Sci.* (1992) 17:277-280; Gehring et al., *Annu. Rev. Genet.* (1986) *20*:147-173; Schofield, *Trends Neurosci.* (1987) *10*:3-6) first

identified in a number of Drosophila homeotic and segmentation proteins. It is extremely well conserved in many other animals, including vertebrates. This domain binds DNA through a helix-turn-helix type of structure. Several proteins that contain a homeobox domain play an important role in development. Most of these proteins are sequence-specific DNA-binding transcription factors. The homeobox domain is also very similar to a region of the yeast mating type proteins. These are sequence-specific DNA-binding proteins that act as master switches in yeast differentiation by controlling gene expression in a cell type-specific fashion.

A schematic representation of the homeobox domain is shown below. The helix-turn-helix region is shown by the symbols 'H' (for helix), and 't' (for turn).

```
xxxxxxxxxxxxxxxxxxxxxxxxxxxxHHHHHHHHHttHHHHHHHHHxxxxxxxxxx
1                                                       60
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The pattern detects homeobox sequences 24 residues long and spans positions 34 to 57 of the homeobox domain. The consensus pattern is as follows: [LIVMFYG]-[ASLVR]-x(2)-[LIVMSTACN]-x-[LIVM]-x(4)-[LIV]-[RKNQESTAIY]-[LIVFSTNKH]-W-[FYVC]-x-[NDQTAH]-x(5)-[RKNAIMW].

<u>MAP kinase kinase (mkk)</u>. SEQ ID NOs:29, 31, 196, 3175, 3190 and 3281 represent novel members of the MAP kinase kinase family. MAP kinases (MAPK) are involved in signal transduction, and are important in cell cycle and cell growth controls. The MAP kinase kinases (MAPKK) are dual-specificity protein kinases which phosphorylate and activate MAP kinases. MAPKK homologues have been found in yeast, invertebrates, amphibians, and mammals. Moreover, the MAPKK/MAPK phosphorylation switch constitutes a basic module activated in distinct pathways in yeast and in vertebrates. MAPKKs are essential transducers through which signals must pass before reaching the nucleus. For review, see, *e.g.*, Biologique *Biol Cell* (1993) *79*:193-207; Nishida et al., *Trends Biochem Sci* (1993) *18*:128-31; Ruderman, *Curr Opin Cell Biol* (1993) *5*:207-13; Dhanasekaran et al., *Oncogene* (1998) *17*:1447-55; Kiefer et al., *Biochem Soc Trans* (1997) *25*:491-8; and Hill, *Cell Signal* (1996) *8*:533-44.

<u>Protein Kinase (protkinase)</u>. SEQ ID NOs:1157, 1478, 1496, 2286, 2969 and 3190 represent polynucleotides encoding protein kinases. Protein kinases catalyze phosphorylation of proteins in a variety of pathways, and are implicated in cancer. Eukaryotic protein kinases (Hanks S.K., et al., *FASEB J.* (1995) 9:576; Hunter T., *Meth. Enzymol.* (1991) *200*:3; Hanks S.K., et al., *Meth. Enzymol.* (1991) *200*:38; Hanks S.K.,

Curr. Opin. Struct. Biol. (1991) *1*:369; Hanks S.K. et al., *Science* (1988) *241*:42) are enzymes that belong to a very extensive family of proteins which share a conserved catalytic core common to both serine/threonine and tyrosine protein kinases. There are a number of conserved regions in the catalytic domain of protein kinases. The first region, which is located in the N-terminal extremity of the catalytic domain, is a glycine-rich stretch of residues in the vicinity of a lysine residue, which has been shown to be involved in ATP binding. The second region, which is located in the central part of the catalytic domain, contains a conserved aspartic acid residue which is important for the catalytic activity of the enzyme (Knighton D.R. et al., *Science* (1991) *253*:407). The protein kinase profile includes two signature patterns for this second region: one specific for serine/threonine kinases and the other for tyrosine kinases. A third profile is based on the alignment in (Hanks S.K. et al., *FASEB J.* (1995) *9*:576) and covers the entire catalytic domain.

The consensus patterns are as follows: 1) [LIV]-G-{P}-G-{P}-[FYWMGSTNH]-[SGA]-{PW}-[LIVCAT]-{PD}-x-[GSTACLIVMFY]-x(5,18)-[LIVMFYWCSTAR]-[AIVP]-[LIVMFAGCKR]-K, where K binds ATP; 2) [LIVMFYC]-x-[HY]-x-D-[LIVMFY]-K-x(2)-N-[LIVMFYCT](3), where D is an active site residue; and 3) [LIVMFYC]-x-[HY]-x-D-[LIVMFY]-[RSTAC]-x(2)-N-[LIVMFYC], where D is an active site residue.

If a protein analyzed includes two of the above protein kinase signatures, the probability of it being a protein kinase is close to 100%.

<u>Ras family proteins (ras)</u>. SEQ ID NOs:1688 and 3258 represent polynucleotides encoding novel members of the ras family of small GTP/GDP-binding proteins (Valencia et al., 1991, Biochemistry 30:4637-4648). Ras family members generally require a specific guanine nucleotide exchange factor (GEF) and a specific GTPase activating protein (GAP) as stimulators of overall GTPase activity. Among ras-related proteins, the highest degree of sequence conservation is found in four regions that are directly involved in guanine nucleotide binding. The first two constitute most of the phosphate and Mg2+ binding site (PM site) and are located in the first half of the G-domain. The other two regions are involved in guanosine binding and are located in the C-terminal half of the molecule. Motifs and conserved structural features of the ras-related proteins are described in Valencia et al., 1991, Biochemistry 30:4637-4648. A major consensus pattern of ras proteins is: D-T-A-G-Q-E-K-[LF]-G-G-L-R-[DE]-G-Y-Y.

Thioredoxin family active site (Thioredox). SEQ ID NO:1677 represents a polynucleotide encoding a protein having a thioredoxin family active site. Thioredoxins (Holmgren A., *Annu. Rev. Biochem.* (1985) *54*:237; Gleason F.K. et al., *FEMS Microbiol. Rev.* (1988) *54*:271; Holmgren, *A. J. Biol. Chem.* (1989) *264*:13963; Eklund H. et al., *Proteins* (1991) *11*:13) are small proteins of approximately one hundred amino- acid residues which participate in various redox reactions via the reversible oxidation of an active center disulfide bond. They exist in either a reduced form or an oxidized form where the two cysteine residues are linked in an intramolecular disulfide bond. Thioredoxin is present in prokaryotes and eukaryotes and the sequence around the redox-active disulfide bond is well conserved. All PDI contains two or three (ERp72) copies of the thioredoxin domain. The consensus pattern is: [LIVMF]-[LIVMSTA]-x-[LIVMFYC]-[FYWSTHE]-x(2)-[FYWGTN]-C-[GATPLVE]-[PHYWSTA]-C-x(6)-[LIVMFYWT] (where the two C's form the redox-active bond).

Trypsin (trypsin). SEQ ID NO:1410 corresponds to a novel serine protease of the trypsin family. The catalytic activity of the serine proteases from the trypsin family is provided by a charge relay system involving an aspartic acid residue hydrogen-bonded to a histidine, which itself is hydrogen-bonded to a serine. The sequences in the vicinity of the active site serine and histidine residues are well conserved in this family of proteases (Brenner S., *Nature* (1988) *334*:528). The consensus patterns for this trypsin protein family are: 1) [LIVM]-[ST]-A-[STAG]-H-C, where H is the active site residue; and 2) [DNSTAGC]-[GSTAPIMVQH]-x(2)-G-[DE]-S-G-[GS]-[SAPHV]- [LIVMFYWH]-[LIVMFYSTANQH], where S is the active site residue. All sequences known to belong to this family are detected by the above consensus sequences, except for 18 different proteases which have lost the first conserved glycine. If a protein includes both the serine and the histidine active site signatures, the probability of it being a trypsin family serine protease is 100%.

WD Domain, G-Beta Repeats (WD domain). SEQ ID NOs:1336, 1380, 1711, 1762, 1909, 2218, 3047, 3108 and 3292 represent novel members of the WD domain/G-beta repeat family. Beta-transducin (G-beta) is one of the three subunits (alpha, beta, and gamma) of the guanine nucleotide-binding proteins (G proteins) which act as intermediaries in the transduction of signals generated by transmembrane receptors (Gilman, *Annu. Rev. Biochem.* (1987) *56*:615). The alpha subunit binds to and hydrolyzes GTP; the functions of the beta and gamma subunits are less clear but they seem to be required for the replacement of GDP by GTP as well as for membrane

anchoring and receptor recognition. In higher eukaryotes, G-beta exists as a small multigene family of highly conserved proteins of about 340 amino acid residues. Structurally, G-beta consists of eight tandem repeats of about 40 residues, each containing a central Trp-Asp motif (this type of repeat is sometimes called a WD-40 repeat). The consensus pattern for the WD domain/G-Beta repeat family is: [LIVMSTAC]-[LIVMFYWSTAGC]-[LIMSTAG]-[LIVMSTAGC]-x(2)-[DN]-x(2)-[LIVMWSTAC]-x-[LIVMFSTAG]-W-[DEN]-[LIVMFSTAGCN].

<u>wnt Family of Developmental Signaling Proteins (Wnt_dev_sign)</u>. SEQ ID NO:1538 corresponds to a novel member of the wnt family of developmental signaling proteins. Wnt-1 (previously known as int-1), the seminal member of this family, (Nusse R., *Trends Genet.* (1988) *4*:291) is thought to play a role in intercellular communication and seems to be a signalling molecule important in the development of the central nervous system (CNS). All wnt family proteins share the following features characteristics of secretory proteins: a signal peptide, several potential N-glycosylation sites and 22 conserved cysteines that are probably involved in disulfide bonds. The Wnt proteins seem to adhere to the plasma membrane of the secreting cells and are therefore likely to signal over only few cell diameters. The consensus pattern, which is based upon a highly conserved region including three cysteines, is as follows: C-K-C-H-G-[LIVMT]-S-G-x-C.

<u>Protein Tyrosine Phosphatase (Y_phosphatase)</u>. SEQ ID NO:1417 represents a polynucleotide encoding a protein tyrosine kinase. Tyrosine specific protein phosphatases (EC 3.1.3.48) (PTPase) (Fischer et al., *Science* (1991) *253*:401; Charbonneau et al., *Annu. Rev. Cell Biol.* (1992) *8*:463; Trowbridge, *J. Biol. Chem.* (1991) *266*:23517; Tonks et al., *Trends Biochem. Sci.* (1989) *14*:497; and Hunter, *Cell* (1989) *58*:1013) catalyze the removal of a phosphate group attached to a tyrosine residue. These enzymes are very important in the control of cell growth, proliferation, differentiation and transformation. Multiple forms of PTPase have been characterized and can be classified into two categories: soluble PTPases and transmembrane receptor proteins that contain PTPase domain(s). Structurally, all known receptor PTPases are made up of a variable length extracellular domain, followed by a transmembrane region and a C-terminal catalytic cytoplasmic domain. PTPase domains consist of about 300 amino acids. The search of two conserved cysteines has been shown to be absolutely required for activity. Furthermore, a number of conserved residues in its immediate vicinity have also been shown to be important. The consensus pattern for PTPases is: [LIVMF]-H-C-x(2)-G-x(3)-[STC]-[STAGP]-x-[LIVMFY]; C is the active site residue.

Zinc Finger, C2H2 Type (Zincfing C2H2). SEQ ID NOs:308, 807, 1324, 1503, 1527, 3081, 3193 and 3306 correspond to polynucleotides encoding novel members of the of the C2H2 type zinc finger protein family. Zinc finger domains (Klug et al., *Trends Biochem. Sci.* (1987) *12*:464; Evans et al., *Cell* (1988) *52*:1; Payre et al., *FEBS Lett.* (1988) *234*:245; Miller et al., *EMBO J.* (1985) *4*:1609; and Berg, *Proc. Natl. Acad. Sci.* USA (1988) *85*:99) are nucleic acid-binding protein structures. In addition to the conserved zinc ligand residues, it has been shown that a number of other positions are also important for the structural integrity of the C2H2 zinc fingers. (Rosenfeld et al., *J. Biomol. Struct. Dyn.* (1993) *11*:557) The best conserved position is found four residues after the second cysteine; it is generally an aromatic or aliphatic residue. The consensus pattern for C2H2 zinc fingers is: C-x(2,4)-C-x(3)-[LIVMFYWC]-x(8)-H-x(3,5)-H. The two C's and two H's are zinc ligands.

Src homology 2. SEQ ID NOs:186, 2591, 3307 and 3339 represent polynucleotides encoding novel members of the family of Src homology 2 (SH2) proteins. The Src homology 2 (SH2) domain is a protein domain of about 100 amino acid residues first identified as a conserved sequence region between the oncoproteins Src and Fps (Sadowski I. et al., *Mol. Cell. Biol. 6*:4396-4408 (1986)). Similar sequences are found in many other intracellular signal-transducing proteins (Russel R.B. et al., *FEBS Lett. 304*:15-20 (1992)). SH2 domains function as regulatory modules of intracellular signalling cascades by interacting with high affinity to phosphotyrosine-containing target peptides in a sequence-specific and phosphorylation-dependent manner (Marangere L.E.M., Pawson T., *J. Cell Sci. Suppl. 18*:97-104 (1994); Pawson T., Schlessinger J., *Curr. Biol. 3*:434-442 (1993); Mayer B.J., Baltimore D., *Trends Cell. Biol. 3*:8-13 (1993); Pawson T., *Nature 373*:573-580 (1995)).

The SH2 domain has a conserved 3D structure consisting of two alpha helices and six to seven beta-strands. The core of the domain is formed by a continuous beta-meander composed of two connected beta-sheets (Kuriyan J., Cowburn D., *Curr. Opin. Struct. Biol. 3*:828-837(1993)). The profile to detect SH2 domains is based on a structural alignment consisting of 8 gap-free blocks and 7 linker regions totaling 92 match positions.

Src homology 3. SEQ ID NO:234, 1832, and 1835 represent polynucleotides encoding novel members of the family of Src homology 3 (SH3) proteins. The Src homology 3 (SH3) domain is a small protein domain of about 60 amino acid residues first identified as a conserved sequence in the non-catalytic part of several cytoplasmic protein tyrosine kinases (*e.g.*, Src, Abl, Lck) (Mayer B.J. et al.,

Nature 332:272-275 (1988)). Since then, it has been found in a great variety of other intracellular or membrane-associated proteins (Musacchio A. et al., *FEBS Lett. 307*:55-61 (1992); Pawson T., Schlessinger J., Curr. Biol. 3:434-442 (1993); Mayer B.J., Baltimore D., *Trends Cell Biol. 3*:8-13 (1993); Pawson T., *Nature 373*:573-580 (1995)).

The SH3 domain has a characteristic fold which consists of five or six beta strands arranged as two tightly packed anti-parallel beta sheets. The linker regions may contain short helices (Kuriyan J., Cowburn D., *Curr. Opin. Struct. Biol. 3*:828-837 (1993)).

The function of the SH3 domain may be to mediate assembly of specific protein complexes via binding to proline-rich peptides (Morton C.J., Campbell I.D., *Curr. Biol. 4*:615-617 (1994)).

In general SH3 domains are found as single copies in a given protein, but there are a significant number of proteins with two SH3 domains and a few with 3 or 4 copies.

<u>Fibronectin type III.</u> SEQ ID NOs:746 and 1192 represent polynucleotides encoding novel members of the family of fibronectin type III proteins. A number of receptors for lymphokines, hematopoeitic growth factors and growth hormone-related molecules have been found to share a common binding domain. (Bazan J.F., *Biochem. Biophys. Res. Commun. 164*:788-795 (1989); Bazan J.F., *Proc. Natl. Acad. Sci. U.S.A. 87*:6934-6938 (1990); Cosman D. et al., *Trends Biochem. Sci. 15*:265-270 (1990); d'Andrea A.D., Fasman G.D., Lodish H.F., *Cell 58*:1023-1024 (1989); d'Andrea A.D., Fasman G.D., Lodish H.F., *Curr. Opin. Cell Biol. 2*:648-651 (1990)).

The conserved region constitutes all or part of the extracellular ligand-binding region and is about 200 amino acid residues long. In the N-terminal of this domain there are two pairs of cysteines known, in the growth hormone receptor, to be involved in disulfide bonds.

```
+-----------------------------------XXXXXXX-------------------------+
|C C          C C       Extracellular    XXXXXXX      Cytoplasmic  | +
-|-|-------|--|----------------------XXXXXXX--------------------------+
 | |        | |                   Transmembrane
 +-+        +--+
```

Two patterns detect this family of receptors. The first one is derived from the first N-terminal disulfide loop, the second is a tryptophan-rich pattern located at the C-terminal extremity of the extracellular region.

A consensus for this protein family is: C-[LVFYR]-x(7,8)-[STIVDN]-C-x-W (The two C's are linked by a disulfide bond]. A second consensus for this protein family is: [STGL]-x-W-[SG]-x-W-S.

LIM domain containing proteins. SEQ ID NOs:1269, 1309, 1360, and 1386 represent polynucleotides encoding novel members of the family of LIM domain containing proteins. A number of proteins contain a conserved cysteine-rich domain of about 60 amino-acid residues. (Freyd G. et al., *Nature 344*:876-879 (1990); Baltz R. et al., *Plant Cell 4*:1465-1466 (1992); Sanchez-Garcia I., Rabbitts T.H., *Trends Genet. 10*:315-320 (1994)).

In the LIM domain, there are seven conserved cysteine residues and a histidine. The arrangement followed by these conserved residues is C-x(2)-C- x(16,23)-H-x(2)-[CH]-x(2)-C-x(2)-C-x(16,21)-C-x(2,3)-[CHD]. The LIM domain binds two zinc ions (Michelsen J.W. et al., *Proc. Natl. Acad. Sci. U.S.A. 90*:4404-4408 (1993)). LIM does not bind DNA, rather it seems to act as interface for protein-protein interaction. The consensus for this protein family is: C-x(2)-C-x(15,21)-[FYWH]-H-x(2)-[CH]-x(2)-C-x(2)-C-x(3)- [LIVMF]. The 5 C's and the H bind zinc.

C2 domain (protein kinase C like). SEQ ID NOs:1325 and 2282 represent polynucleotides encoding novel members of the family of C2 domain containing proteins. Some isozymes of protein kinase C (PKC) contain a domain, known as C2, of about 116 amino-acid residues, which is located between the two copies of the C1 domain (that bind phorbol esters and diacylglycerol) and the protein kinase catalytic domain. (Azzi A. et al., *Eur. J. Biochem. 208*:547-557 (1992); Stabel S., Semin. Cancer Biol. 5:277-284 (1994)).

The C2 domain is involved in calcium-dependent phospholipid binding (Davletov B.A., Suedhof T.C., *J. Biol. Chem. 268*:26386-26390 (1993)). Since domains related to the C2 domain are also found in proteins that do not bind calcium, other putative functions for the C2 domain include binding to inositol-1,3,5-tetraphosphate. (Fukuda M., et al., *J. Biol. Chem. 269*:29206-29211 (1994).)

The consensus pattern for the C2 domain is located in a conserved part of that domain, the connecting loop between beta strands 2 and 3. The profile for the C2 domain covers the total domain. The consensus for this protein family is:: [ACG]-x(2)-L-x(2,3)-D-x(1,2)-[NGSTLIF]-[GTMR]-x-[STAP]-D- [PA]-[FY]

Serine proteases, trypsin family, active sites. SEQ ID NO:1410 represents a polynucleotide encoding a novel member of the family of serine protease, trypsin proteins. The catalytic activity of the serine proteases from the trypsin family is

provided by a charge relay system involving an aspartic acid residue hydrogen-bonded to a histidine, which itself is hydrogen-bonded to a serine. The sequences in the vicinity of the active site serine and histidine residues are well conserved in this family of proteases (Brenner S., *Nature 334*:528-530 (1988)).

A consensus for this protein family is: [LIVM]-[ST]-A-[STAG]-H-C [H is the active site residue]. A second consensus for this protein family is: [DNSTAGC]-[GSTAPIMVQH]-x(2)-G-[DE]-S-G-[GS]-[SAPHV]- [LIVMFYWH]-[LIVMFYSTANQH] [S is the active site residue].

<u>RNA Recognition Motif Domain (RRM, RBD, or RNP).</u> SEQ ID NOs: 1464 and 1514 represent polynucleotides encoding novel members of the family of RNA recognition motif domain proteins (Bandziulis R.J. et al., *Genes Dev. 3*:431-437 (1989); Dreyfuss G. et al., *Trends Biochem. Sci. 13*:86-91 (1988)).

Inside the putative RNA-binding domain there are two regions which are highly conserved. The first one is a hydrophobic segment of six residues (which is called the RNP-2 motif); the second one is an octapeptide motif (which is called RNP-1 or RNP-CS). The position of both motifs in the domain is shown in the following schematic representation:

```
xxxxxxx######xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx########xxxxxxxxxxxxxxxxxxxxxxxxxx
         RNP-2                                    RNP-1
```

As a consensus pattern for this type of domain the RNP-1 motif was used. The consensus for this protein family is: [RK]-G-{EDRKHPCG}-[AGSCI]-[FY]-[LIVA]-x-[FYLM]

<u>Phosphatidylinositol-specific phospholipase C, Y Domain.</u> SEQ ID NO: 1707 represents a polynucleotide encoding a novel member of the phosphatidylinositol-specific phospholipase C, Y domain family of proteins. Phosphatidylinositol-specific phospholipase C (EC3.1.4.11), a eukaryotic intracellular enzyme, plays an important role in signal transduction processes (Meldrum E. et al., *Biochim. Biophys. Acta 1092*:49-71 (1991)). It catalyzes the hydrolysis of 1-phosphatidyl-D-myo-inositol-3,4,5- triphosphate into the second messenger molecules diacylglycerol and inositol-1,4,5-triphosphate. This catalytic process is tightly regulated by reversible phosphorylation and binding of regulatory proteins (Rhee S.G., Choi K.D., *Adv. Second Messenger Phosphoprotein Res. 26*:35-61 (1992); Rhee S.G., Choi K.D., *J. Biol. Chem. 267*:12393-12396 (1992); Sternweis P.C., Smrcka A.V., Trends Biochem. *Sci. 17*:502-506 (1992)).

All eukaryotic PI-PLCs contain two regions of homology, referred to as "X-box" and "Y-box". The order of these two regions is the same (NH2-X-Y-COOH), but the spacing is variable. In most isoforms, the distance between these two regions is only 50-100 residues but in the gamma isoforms one PH domain, two SH2 domains, and one SH3 domain are inserted between the two PLC-specific domains. The two conserved regions have been shown to be important for the catalytic activity. At the C-terminal of the Y-box, there is a C2 domain possibly involved in Ca-dependent membrane attachment.

<u>Serine Carboxypeptidases.</u> SEQ ID NO:1744 represents a polynucleotide encoding a novel member of the serine carboxypeptidases family of proteins. Carboxypeptidases may be either metallo carboxypeptidases or serine carboxypeptidases (EC 3.4.16.5 and EC 3.4.16.6). The catalytic activity of the serine carboxypeptidases, like that of the trypsin family serine proteases, is provided by a charge relay system involving an aspartic acid residue hydrogen-bonded to a histidine, which is itself hydrogen-bonded to a serine (Liao D.I., Remington S.J., *J. Biol. Chem. 265*:6528-6531 (1990)).

The sequences surrounding the active site serine and histidine residues are highly conserved in all these serine carboxypeptidases. A consensus for this protein family is: [LIVM]-x-[GTA]-E-S-Y-[AG]-[GS] [S is the active site residue]. A second consensus for this protein family is: [LIVF]-x(2)-[LIVSTA]-x-[IVPST]-x-[GSDNQL]-[SAGV]-[SG]-H-x- [IVAQ]-P-x(3)-[PSA] [H is the active site residue].

<u>dsrm Double-Stranded RNA Binding Motif.</u> SEQ ID NO:1818 represents a polynucleotide encoding a novel member of the dsrm double-stranded RNA binding motif proteins. In eukaryotic cells, a multitude of RNA-binding proteins play key roles in the posttranscriptional regulation of gene expression. Characterization of these proteins has led to the identification of several RNA-binding motifs. Several human and other vertebrate genetic disorders are caused by aberrant expression of RNA-binding proteins. (C. G. Burd & G. Dreyfuss, *Science 265*: 615-621 (1994)).

Proteins containing double stranded RNA binding motifs bind to specific RNA targets. Double stranded RNA binding motifs are exemplified by interferon-induced protein kinase in humans, which is part of the cellular response to dsRNA.

SEQ ID NOs:2577, 3183 and 3195 encode members of the 4 trans-membrane integral membrane protein family. This family consists of type III proteins, which are integral membrane proteins that contain a N-terminal membrane-anchoring domain that is not cleaved during biosynthesis, and which functions as a translocation

signal and a membrane anchor. The proteins also have three additional transmembrane regions. The consensus pattern is: G-x(3)-[LIVMF]-x(2)-[GSA]-[LIVMF] (2)-G-C-x-[GA]-[STA]-x(20-[eG]-x(20-[CwN]-[LIVM](2).

SEQ ID NO:2944 encodes a polypeptide having a calpain large subunit, domain III. Calpains are a family of intracellular proteases that play a variety of biological roles. Calpain 3, also known as p94, is predominantly expressed in skeletal muscle and plays a role in limb-girdle muscular dystrophy type 2A. (Sorimachi, H. et al., Biochem. J. 328:721-732, 1997).

SEQ ID NOs:1911 and 1980 encode polypeptides having a C3HC4 type zinc finger domain (RING finger), which is a cysteine-rich domain of 40 to 60 residues that binds two atoms of zinc, and is believed to be involved in mediating protein-protein interactions. Mammalian proteins of this family include V(D)J recombination activating protein, which activates the rearrangement of immunoglobulin and T-cell receptor genes; breast cancer type 1 susceptibility protein (BRCA1); bmi-1 proto-oncogene; cbl proto-oncogene; and mel-18 protein, which is expressed in a variety of tumor cells and is a transcriptional repressor that recognizes and binds a specific DNA sequence. The consensus pattern is: C-x-H-x-[LIVMFY]-C-x(2)-C-[LIVMYA].

SEQ ID NO:3274 encodes a eukaryotic transcription factor with a fork head domain, of about 100 amino acid residues. Proteins of this group are transcription factors, including mammalian transcription factors HNF-3-alpha, -beta, and -gamma; interleukin-enhancer binding factor; and HTLF, which binds to a region of human T-cell leukemia virus long terminal repeat. The consensus pattern is [KR]-P-[PTQ]-[FYLVQH]-S-[FY]x(2)-[LIVM]-X(3,4)-[AC]-[LIM].

SEQ ID NO:3345 encodes a polypeptide having a PDZ domain. Several dozen signaling proteins belong to this group of proteins that have 80-100 residue repeats known as PDZ domains. Several of the proteins interact with the C-terminal tetrapeptide motifs X-Ser/Thr/X-Val-COO- of ion channels and/or receptors. (Ponting, C. P., Protein Sci. 6;464-468, 1997.)

SEQ ID NO:3351 encodes a polypeptide in the family of phorbol esters/glycerol binding proteins. Phorbol esters (PE) are analogues of diacylglycerol (DAG) and potent tumor promoters. DAG activates a family of serine-threonine protein kinases, known as protein kinase C. The N-terminal region of protein kinase C binds PE and DAG, and contains one or two copies of a cysteine-rich domain of about 50 amino acid residues. Other proteins having this domain include diacylglycerol kinase; the vav oncogene; and N-chimaerin, a brain-specific protein. The DAG/PE binding

domain binds two zinc ions through the six cysteines and two histidines that are conserved in the domain. The consensus pattern is: H-x-[LIVMFYW]-x(8, 11)-C-x(2)-C-x-(3)-[LIVMFC]-x(5, 10)-C-x(2)-C-x(4)-[HD]-x(2)-C-x(5, 9)-C.

SEQ ID NO:2216 encodes a polypeptide having a WW/rsp5/WWP domain. The protein is named for the presence of conserved aromatic positions, generally tryptophan, as well as a conserved proline. Proteins having the domain include dystrophin, vertebrate YAP protein, and IQGAP, a human GTPase activating protein which acts on ras. The consensus pattern is: W-x(9,11)-[VFY]-[FYW]-x(6,7)-[GSTNE]-[GSTQCR]-[FYW]-x(2)-P.

SEQ ID NO:2428 encodes a member of the dual specificity phosphatase family, having a catalytic domain, and SEQ IDS NOs:2281 and 2310 encode members of the protein tyrosine phosphatase family. These families are related and classified as tyrosine specific protein phosphatases. The enzymes catalyze the removal of a phosphate group from a tyrosine residue, and are important in the control of cell growth, proliferation, differentiation, and transformation. The consensus pattern is [LIVMF]-H-C-x(2)-G-x-(3)-[STC]-[STAGP]-x-[LIVMFY].

Table 1

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2	377708	RTA00002683F.m.01.2.P.Seq	F	M00040089A:G08	CH09LNL
3	427782	RTA00002666F.l.06.1.P.Seq	F	M00032638D:A06	CH08LNH
4	29372	RTA00002712F.a.06.1.P.Seq	F	M00023282A:C02	CH04MAL
5	455003	RTA00002694F.b.02.1.P.Seq	F	M00043419D:A10	CH20COHLV
6	380625	RTA00002684F.d.03.2.P.Seq	F	M00040118D:G10	CH09LNL
7	450959	RTA00002691F.b.05.3.P.Seq	F	M00043306D:B07	CH17COHLV
8	397851	RTA00002680F.b.04.1.P.Seq	F	M00039775A:A09	CH09LNL
9	20652	RTA00002710F.k.01.1.P.Seq	F	M00022440B:E01	CH03MAH
10	97830	RTA00002663F.k.18.1.P.Seq	F	M00022767B:G11	CH03MAH
11	373071	RTA00002670F.j.23.1.P.Seq	F	M00033442A:D06	CH09LNL
12	162369	RTA00002713F.e.01.1.P.Seq	F	M00027292D:F10	CH04MAL
13	401247	RTA00002685F.f.15.2.P.Seq	F	M00039508A:C12	CH12EDT
14	430738	RTA00002669F.i.15.3.P.Seq	F	M00033231D:B09	CH08LNH
15	46779	RTA00002711F.c.14.1.P.Seq	F	M00022860C:G04	CH03MAH
16	375772	RTA00002681F.p.01.2.P.Seq	F	M00039909C:G05	CH09LNL
17	430689	RTA00002669F.j.01.3.P.Seq	F	M00033243B:A05	CH08LNH
18	376546	RTA00002677F.d.07.2.P.Seq	F	M00039345C:C12	CH09LNL
19	430041	RTA00002667F.f.17.1.P.Seq	F	M00032790B:A07	CH08LNH
20	431643	RTA00002669F.l.16.1.P.Seq	F	M00033276D:H09	CH08LNH
21	19422	RTA00002709F.c.02.1.P.Seq	F	M00005449B:B10	CH02COH
22	376802	RTA00002677F.c.18.2.P.Seq	F	M00039344B:G07	CH09LNL
23	376814	RTA00002674F.h.02.1.P.Seq	F	M00039139C:G12	CH09LNL
24	375492	RTA00002677F.m.19.2.P.Seq	F	M00039418B:D08	CH09LNL
25	379114	RTA00002681F.n.24.2.P.Seq	F	M00039903C:F03	CH09LNL
26	380668	RTA00002670F.p.11.1.P.Seq	F	M00033581C:H10	CH09LNL
27	213817	RTA00002664F.i.19.2.P.Seq	F	M00027634A:D11	CH04MAL
28	375749	RTA00002680F.f.23.1.P.Seq	F	M00039795D:G06	CH09LNL
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30	380462	RTA00002670F.o.01.1.P.Seq	F	M00033570B:E06	CH09LNL
31	430896	RTA00002669F.b.20.3.P.Seq	F	M00033185C:D01	CH08LNH
32	376996	RTA00002676F.p.13.2.P.Seq	F	M00039329C:B10	CH09LNL
33	374846	RTA00002677F.k.19.2.P.Seq	F	M00039412D:G06	CH09LNL
34	379075	RTA00002672F.n.13.2.P.Seq	F	M00039039B:E03	CH09LNL
35	374172	RTA00002673F.k.16.2.P.Seq	F	M00039097D:D06	CH09LNL
36	373104	RTA00002683F.o.15.2.P.Seq	F	M00040098D:G12	CH09LNL
37	186302	RTA00002713F.m.21.1.P.Seq	F	M00027591B:C04	CH04MAL
38	427947	RTA00002665F.o.01.1.P.Seq	F	M00032495B:D02	CH08LNH
39	375180	RTA00002673F.d.17.1.P.Seq	F	M00039064D:H09	CH09LNL
40	377584	RTA00002683F.l.22.2.P.Seq	F	M00040088C:E10	CH09LNL
41	377364	RTA00002678F.a.15.2.P.Seq	F	M00039432C:A01	CH09LNL
42	376347	RTA00002675F.l.08.1.P.Seq	F	M00039249C:G11	CH09LNL
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44	28092	RTA00002711F.g.12.1.P.Seq	F	M00023032A:B05	CH03MAH
45	378206	RTA00002671F.a.20.3.P.Seq	F	M00033588C:G04	CH09LNL
46	378206	RTA00002671F.a.20.2.P.Seq	F	M00033588C:G04	CH09LNL
47	14940	RTA00002709F.d.11.1.P.Seq	F	M00005623A:G02	CH02COH

SEQ ID	CLUSTER	SEQ NAME	ORIENTATION	CLONE ID	LIBRARY
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49	38120	RTA00002712F.i.14.1.P.Seq	F	M00026927D:F02	CH04MAL
50	375730	RTA00002678F.l.13.2.P.Seq	F	M00039612B:G05	CH09LNL
51	428959	RTA00002667F.h.15.1.P.Seq	F	M00032811B:D02	CH08LNH
52	376851	RTA00002677F.c.03.2.P.Seq	F	M00039341C:H11	CH09LNL
53	373808	RTA00002671F.d.14.2.P.Seq	F	M00038272A:G01	CH09LNL
54	376168	RTA00002675F.n.17.1.P.Seq	F	M00039258B:E06	CH09LNL
55	18653	RTA00002712F.o.08.1.P.Seq	F	M00027135A:B11	CH04MAL
56	187632	RTA00002664F.i.15.1.P.Seq	F	M00027617B:C12	CH04MAL
57	374122	RTA00002673F.l.22.1.P.Seq	F	M00039104D:C09	CH09LNL
58	374946	RTA00002673F.j.24.1.P.Seq	F	M00039096A:E07	CH09LNL
59	375666	RTA00002677F.n.16.2.P.Seq	F	M00039422D:F04	CH09LNL
60	162369	RTA00002713F.d.24.1.P.Seq	F	M00027292D:F10	CH04MAL
61	21480	RTA00002709F.c.18.2.P.Seq	F	M00005531D:F06	CH02COH
62	18560	RTA00002711F.e.20.1.P.Seq	F	M00022938B:F07	CH03MAH
63	96575	RTA00002663F.j.08.1.P.Seq	F	M00022641C:H05	CH03MAH
64	377576	RTA00002682F.f.18.1.P.Seq	F	M00039975C:C11	CH09LNL
65	446747	RTA00002689F.d.16.3.P.Seq	F	M00042740A:E09	CH15CON
66	379311	RTA00002682F.g.01.1.P.Seq	F	M00039976D:A12	CH09LNL
67	379311	RTA00002682F.f.24.1.P.Seq	F	M00039976D:A12	CH09LNL
68	124549	RTA00002713F.c.07.1.P.Seq	F	M00027237C:B08	CH04MAL
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82	17253	RTA00002709F.h.23.1.P.Seq	F	M00006866A:D07	CH02COH
83	21565	RTA00002709F.e.11.1.P.Seq	F	M00005778B:F09	CH02COH
84	373996	RTA00002673F.n.11.1.P.Seq	F	M00039108D:B06	CH09LNL
85	380437	RTA00002683F.c.09.1.P.Seq	F	M00040039D:D06	CH09LNL
86	430729	RTA00002669F.h.18.2.P.Seq	F	M00033226A:A11	CH08LNH
87	376791	RTA00002674F.l.17.1.P.Seq	F	M00039166B:G06	CH09LNL
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89	373837	RTA00002672F.p.22.1.P.Seq	F	M00039050A:H10	CH09LNL
90	376435	RTA00002678F.h.17.2.P.Seq	F	M00039476B:A02	CH09LNL
91	373881	RTA00002672F.b.20.1.P.Seq	F	M00038638D:H03	CH09LNL
92	377086	RTA00002676F.p.07.1.P.Seq	F	M00039328D:D07	CH09LNL
93	377889	RTA00002672F.c.08.1.P.Seq	F	M00038661A:A07	CH09LNL
94	380442	RTA00002684F.b.05.2.P.Seq	F	M00040111C:D05	CH09LNL

SEQ ID	CLUSTER	SEQ NAME	ORIENTATION	CLONE ID	LIBRARY
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96	375339	RTA00002678F.m.23.2.P.Seq	F	M00039616A:B10	CH09LNL
97	14197	RTA00002710F.f.15.1.P.Seq	F	M00022084D:B01	CH03MAH
98	380666	RTA00002684F.c.04.2.P.Seq	F	M00040115B:H12	CH09LNL
99	377352	RTA00002677F.i.13.2.P.Seq	F	M00039404B:A05	CH09LNL
100	379188	RTA00002682F.a.03.1.P.Seq	F	M00039914D:G12	CH09LNL
101	428269	RTA00002666F.c.13.1.P.Seq	F	M00032539B:C11	CH08LNH
102	373464	RTA00002671F.l.13.3.P.Seq	F	M00038327A:C11	CH09LNL
103	15527	RTA00002710F.p.07.1.P.Seq	F	M00022747D:E03	CH03MAH
104	377504	RTA00002671F.i.17.3.P.Seq	F	M00038303C:D02	CH09LNL
105	33508	RTA00002710F.g.17.1.P.Seq	F	M00022183B:C02	CH03MAH
106	129179	RTA00002662F.d.19.2.P.Seq	F	M00007157C:F11	CH02COH
107	377086	RTA00002676F.p.07.2.P.Seq	F	M00039328D:D07	CH09LNL
108	375872	RTA00002675F.h.15.1.P.Seq	F	M00039233A:A03	CH09LNL
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521	373607	RTA00002674F.d.15.2.P.Seq	F	M00039127D:E10	CH09LNL
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621	376485	RTA00002676F.e.24.2.P.Seq	F	M00039288C:B11	CH09LNL
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635	402817	RTA00002686F.a.10.1.P.Seq	F	M00039736D:G08	CH13EDT
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652	240615	RTA00002672F.e.19.1.P.Seq	F	M00038995D:E05	CH09LNL
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929	454453	RTA00002693F.f.15.2.P.Seq	F	M00043215A:D02	CH19COP
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938	450463	RTA00002694F.a.12.1.P.Seq	F	M00042596C:D07	CH20COHLV
939	456713	RTA00002694F.d.13.1.P.Seq	F	M00043513D:G08	CH20COHLV
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992	373874	RTA00002672F.c.22.2.P.Seq	F	M00038663D:H10	CH09LNL
993	401050	RTA00002685F.e.09.2.P.Seq	F	M00039499C:A04	CH12EDT
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997	378014	RTA00002680F.g.17.2.P.Seq	F	M00039799A:D10	CH09LNL
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1040	406092	RTA00002685F.k.11.1.P.Seq	F	M00039584C:C11	CH12EDT
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1042	402365	RTA00002686F.j.08.1.P.Seq	F	M00040230A:H02	CH13EDT
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1044	447669	RTA00002689F.a.15.2.P.Seq	F	M00042533B:E06	CH15CON
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1049	402952	RTA00002686F.g.14.1.P.Seq	F	M00040181D:H10	CH13EDT
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1053	403242	RTA00002687F.l.05.1.P.Seq	F	M00040323B:C12	CH14EDT
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1055	449269	RTA00002690F.c.12.3.P.Seq	F	M00042770B:B12	CH16COP
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1126	453019	RTA00002692F.d.18.2.P.Seq	F	M00043015A:H10	CH18CON
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1137	45505	RTA00002712F.d.04.1.P.Seq	F	M00023377B:F01	CH04MAL
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1171	403912	RTA00002687F.j.19.2.P.Seq	F	M00040317A:H03	CH14EDT
1172	401471	RTA00002685F.o.10.2.P.Seq	F	M00039629B:F01	CH12EDT
1173	404362	RTA00002687F.o.06.1.P.Seq	F	M00040342B:D12	CH14EDT
1174	403849	RTA00002687F.n.09.1.P.Seq	F	M00040333D:G05	CH14EDT
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1180	403898	RTA00002687F.a.05.1.P.Seq	F	M00039746C:H06	CH14EDT
1181	453512	RTA00002693F.a.21.2.P.Seq	F	M00043078D:D04	CH19COP
1182	404172	RTA00002687F.d.17.1.P.Seq	F	M00039951B:B12	CH14EDT
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1185	451502	RTA00002691F.f.03.2.P.Seq	F	M00043406B:G12	CH17COHLV
1186	454414	RTA00002693F.f.18.2.P.Seq	F	M00043220B:C04	CH19COP
1187	453752	RTA00002693F.b.02.2.P.Seq	F	M00043081D:F05	CH19COP
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1191	404161	RTA00002687F.e.20.1.P.Seq	F	M00039958C:B09	CH14EDT
1192	403274	RTA00002687F.b.10.1.P.Seq	F	M00039766A:G07	CH14EDT
1193	373465	RTA00002671F.o.09.1.P.Seq	F	M00038615A:H12	CH09LNL
1194	402582	RTA00002686F.m.08.1.P.Seq	F	M00040265D:C08	CH13EDT
1195	402241	RTA00002686F.l.16.1.P.Seq	F	M00040261C:F01	CH13EDT
1196	380451	RTA00002670F.p.12.1.P.Seq	F	M00033581D:D08	CH09LNL
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1217	400147	RTA00002685F.g.10.2.P.Seq	F	M00039515A:A06	CH12EDT
1218	401655	RTA00002685F.c.22.2.P.Seq	F	M00039378D:H07	CH12EDT
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1221	451718	RTA00002692F.e.24.1.P.Seq	F	M00043044B:A12	CH18CON
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1226	450773	RTA00002691F.d.24.3.P.Seq	F	M00043383D:A02	CH17COHLV
1227	376236	RTA00002685F.l.24.2.P.Seq	F	M00039595C:E05	CH12EDT
1228	422357	RTA00002688F.c.21.1.P.Seq	F	M00040385C:D02	CH14EDT
1229	404532	RTA00002687F.p.10.2.P.Seq	F	M00040351B:F02	CH14EDT
1230	403693	RTA00002687F.j.23.1.P.Seq	F	M00040317D:F02	CH14EDT
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1232	401515	RTA00002685F.o.02.2.P.Seq	F	M00039624B:F12	CH12EDT
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1235	18003	RTA00002711F.b.04.1.P.Seq	F	M00022821C:C09	CH03MAH
1236	377014	RTA00002682F.f.13.1.P.Seq	F	M00039973D:C08	CH09LNL
1237	404232	RTA00002687F.n.12.2.P.Seq	F	M00040334D:C07	CH14EDT
1238	404232	RTA00002687F.n.12.1.P.Seq	F	M00040334D:C07	CH14EDT
1239	406263	RTA00002685F.d.14.1.P.Seq	F	M00039493A:C04	CH12EDT
1240	452077	RTA00002692F.c.24.2.P.Seq	F	M00043002A:E05	CH18CON
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1245	401827	RTA00002686F.l.19.1.P.Seq	F	M00040262B:B06	CH13EDT
1246	404520	RTA00002687F.f.05.1.P.Seq	F	M00040202A:F05	CH14EDT
1247	449798	RTA00002691F.d.02.3.P.Seq	F	M00043366A:A02	CH17COHLV
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1260	453011	RTA00002692F.f.10.1.P.Seq	F	M00043066B:H11	CH18CON
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1262	379602	RTA00002681F.c.21.2.P.Seq	F	M00039855C:F01	CH09LNL
1263	403896	RTA00002687F.a.04.1.P.Seq	F	M00039746C:H05	CH14EDT
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1268	375483	RTA00002686F.n.14.1.P.Seq	F	M00040274A:D07	CH13EDT
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1274	54656	RTA00002661F.i.22.2.P.Seq	F	M00004372B:F07	CH01COH
1275	379183	RTA00002679F.i.17.1.P.Seq	F	M00039688C:G06	CH09LNL
1276	25594	RTA00002711F.f.07.1.P.Seq	F	M00022968B:E02	CH03MAH
1277	403355	RTA00002687F.d.11.1.P.Seq	F	M00039948D:D11	CH14EDT
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1293	12926	RTA00002710F.e.21.1.P.Seq	F	M00022005C:C06	CH03MAH
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1305	403355	RTA00002687F.d.11.2.P.Seq	F	M00039948D:D11	CH14EDT
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1307	222658	RTA00002664F.e.14.2.P.Seq	F	M00027103B:A09	CH04MAL
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1310	455579	RTA00002694F.a.10.1.P.Seq	F	M00042596B:F06	CH20COHLV
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1312	378364	RTA00002674F.o.17.1.P.Seq	F	M00039196D:A07	CH09LNL
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1315	22425	RTA00002709F.c.08.2.P.Seq	F	M00005498A:H06	CH02COH
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1321	380355	RTA00002670F.o.06.1.P.Seq	F	M00033570C:C10	CH09LNL
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1323	378952	RTA00002683F.h.11.1.P.Seq	F	M00040070B:B07	CH09LNL
1324	404487	RTA00002687F.c.13.2.P.Seq	F	M00039943B:F10	CH14EDT
1325	48482	RTA00002712F.p.06.1.P.Seq	F	M00027159D:F03	CH04MAL
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1330	21162	RTA00002709F.c.03.2.P.Seq	F	M00005449B:D01	CH02COH
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1351	455957	RTA00002694F.c.15.1.P.Seq	F	M00043465C:A03	CH20COHLV
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1361	377206	RTA00002682F.m.14.1.P.Seq	F	M00040015C:F08	CH09LNL
1362	453036	RTA00002692F.b.11.2.P.Seq	F	M00042960D:H08	CH18CON
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1367	379011	RTA00002681F.n.23.1.P.Seq	F	M00039903C:D01	CH09LNL
1368	404048	RTA00002687F.g.01.1.P.Seq	F	M00040206A:A07	CH14EDT
1369	404048	RTA00002687F.g.01.2.P.Seq	F	M00040206A:A07	CH14EDT
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1377	379011	RTA00002681F.n.23.2.P.Seq	F	M00039903C:D01	CH09LNL
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1379	427346	RTA00002665F.a.24.3.P.Seq	F	M00028066C:D07	CH08LNH
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1388	403796	RTA00002687F.h.17.1.P.Seq	F	M00040293D:G04	CH14EDT
1389	452314	RTA00002694F.a.21.1.P.Seq	F	M00043416C:A02	CH20COHLV
1390	119179	RTA00002712F.k.20.1.P.Seq	F	M00027021A:G02	CH04MAL
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1393	289535	RTA00002693F.f.06.1.P.Seq	F	M00043202B:F01	CH19COP
1394	374736	RTA00002673F.o.08.2.P.Seq	F	M00039112B:C05	CH09LNL
1395	378912	RTA00002672F.n.01.2.P.Seq	F	M00039036C:B05	CH09LNL
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1403	212635	RTA00002666F.o.24.1.P.Seq	F	M00032688D:D11	CH08LNH
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1407	431066	RTA00002669F.c.17.3.P.Seq	F	M00033189D:F08	CH08LNH
1408	378912	RTA00002672F.m.24.2.P.Seq	F	M00039036C:B05	CH09LNL
1409	15731	RTA00002709F.l.13.1.P.Seq	F	M00007116C:G02	CH02COH
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1413	379942	RTA00002679F.l.21.1.P.Seq	F	M00039707A:D02	CH09LNL
1414	375589	RTA00002680F.f.06.1.P.Seq	F	M00039794A:E04	CH09LNL
1415	375789	RTA00002674F.a.16.1.P.Seq	F	M00039120C:H03	CH09LNL
1416	456227	RTA00002694F.c.16.1.P.Seq	F	M00043465C:C09	CH20COHLV
1417	455852	RTA00002694F.a.02.1.P.Seq	F	M00042592A:H10	CH20COHLV
1418	25169	RTA00002710F.m.05.1.P.Seq	F	M00022579C:C11	CH03MAH
1419	376524	RTA00002678F.h.23.2.P.Seq	F	M00039477A:B03	CH09LNL
1420	449562	RTA00002690F.b.13.2.P.Seq	F	M00042515C:F08	CH16COP
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1425	401603	RTA00002685F.f.23.2.P.Seq	F	M00039510C:G02	CH12EDT
1426	376541	RTA00002678F.d.13.2.P.Seq	F	M00039456A:C08	CH09LNL
1427	449123	RTA00002690F.a.13.3.P.Seq	F	M00042435A:A11	CH16COP
1428	418358	RTA00002686F.m.07.1.P.Seq	F	M00040265D:B07	CH13EDT
1429	380263	RTA00002689F.a.22.1.P.Seq	F	M00042543C:G04	CH15CON
1430	455748	RTA00002694F.b.06.1.P.Seq	F	M00043428D:G08	CH20COHLV
1431	451679	RTA00002693F.a.04.2.P.Seq	F	M00042612D:F06	CH19COP
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1435	402494	RTA00002686F.h.16.1.P.Seq	F	M00040191A:B09	CH13EDT
1436	372798	RTA00002670F.c.18.2.P.Seq	F	M00033349D:F05	CH09LNL
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1440	455706	RTA00002694F.b.10.1.P.Seq	F	M00043433B:G09	CH20COHLV
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1446	117060	RTA00002679F.h.24.1.P.Seq	F	M00039686C:C05	CH09LNL
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1448	448589	RTA00002690F.a.07.3.P.Seq	F	M00042349D:D07	CH16COP
1449	373806	RTA00002674F.o.02.1.P.Seq	F	M00039179A:G09	CH09LNL
1450	377055	RTA00002682F.k.13.1.P.Seq	F	M00040005B:C11	CH09LNL
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1455	403200	RTA00002687F.k.01.2.P.Seq	F	M00040318A:B02	CH14EDT
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1461	401013	RTA00002685F.o.16.1.P.Seq	F	M00039641A:A05	CH12EDT
1462	74344	RTA00002661F.f.10.1.P.Seq	F	M00003902A:C03	CH01COH
1463	423432	RTA00002687F.l.10.2.P.Seq	F	M00040323C:G11	CH14EDT
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1481	403232	RTA00002687F.g.20.1.P.Seq	F	M00040218C:C02	CH14EDT
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1484	374742	RTA00002676F.c.12.2.P.Seq	F	M00039279B:C11	CH09LNL
1485	449741	RTA00002690F.e.23.2.P.Seq	F	M00042856B:H02	CH16COP
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1487	451220	RTA00002691F.f.07.2.P.Seq	F	M00043408B:D11	CH17COHLV
1488	22067	RTA00002708F.f.12.1.P.Seq	F	M00004140D:C03	CH01COH
1489	378952	RTA00002683F.h.11.2.P.Seq	F	M00040070B:B07	CH09LNL
1490	401435	RTA00002685F.n.14.2.P.Seq	F	M00039607D:E08	CH12EDT
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1509	447859	RTA00002689F.d.13.1.P.Seq	F	M00042737C:H04	CH15CON
1510	452572	RTA00002692F.e.16.1.P.Seq	F	M00043034D:C01	CH18CON
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1516	229665	RTA00002664F.c.08.2.P.Seq	F	M00026885A:H09	CH04MAL
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1518	448841	RTA00002690F.d.10.3.P.Seq	F	M00042799D:F08	CH16COP
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1525	450149	RTA00002692F.a.20.2.P.Seq	F	M00042630A:C05	CH18CON
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1528	375243	RTA00002680F.e.01.2.P.Seq	F	M00039788C:A01	CH09LNL
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1530	373647	RTA00002672F.d.04.2.P.Seq	F	M00038664C:E04	CH09LNL
1531	376897	RTA00002674F.l.20.1.P.Seq	F	M00039167B:H09	CH09LNL
1532	23468	RTA00002708F.e.02.1.P.Seq	F	M00003991C:F06	CH01COH
1533	455184	RTA00002694F.a.05.1.P.Seq	F	M00042593A:C02	CH20COHLV
1534	455327	RTA00002694F.a.22.1.P.Seq	F	M00043417C:D05	CH20COHLV
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1536	455688	RTA00002694F.c.18.1.P.Seq	F	M00043476A:F07	CH20COHLV
1537	456286	RTA00002694F.b.23.1.P.Seq	F	M00043450C:C06	CH20COHLV
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1541	455319	RTA00002694F.b.13.1.P.Seq	F	M00043437D:D04	CH20COHLV
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1543	451814	RTA00002692F.e.20.2.P.Seq	F	M00043040B:B07	CH18CON
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1547	451981	RTA00002692F.c.23.2.P.Seq	F	M00043001D:D03	CH18CON
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1564	456522	RTA00002694F.e.16.1.P.Seq	F	M00043649B:E07	CH20COHLV
1565	379167	RTA00002692F.c.09.2.P.Seq	F	M00042983C:A11	CH18CON
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1567	450956	RTA00002691F.b.04.3.P.Seq	F	M00043306C:B03	CH17COHLV
1568	448999	RTA00002690F.d.08.3.P.Seq	F	M00042792A:H01	CH16COP
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1570	414331	RTA00002685F.c.14.1.P.Seq	F	M00039376D:H07	CH12EDT
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1572	174250	RTA00002689F.c.09.1.P.Seq	F	M00042697D:C07	CH15CON
1573	448991	RTA00002690F.d.02.3.P.Seq	F	M00042784A:H06	CH16COP
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1577	448853	RTA00002690F.b.03.3.P.Seq	F	M00042463A:F09	CH16COP
1578	449496	RTA00002690F.e.06.2.P.Seq	F	M00042830B:E02	CH16COP
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1580	451297	RTA00002691F.f.05.1.P.Seq	F	M00043407C:E05	CH17COHLV
1581	289519	RTA00002691F.d.18.2.P.Seq	F	M00043378A:H10	CH17COHLV
1582	448933	RTA00002693F.c.05.2.P.Seq	F	M00043109C:G01	CH19COP
1583	450806	RTA00002691F.c.14.3.P.Seq	F	M00043351D:A11	CH17COHLV
1584	450452	RTA00002691F.d.07.3.P.Seq	F	M00043368C:F09	CH17COHLV
1585	450754	RTA00002691F.d.03.2.P.Seq	F	M00043366C:H05	CH17COHLV
1586	452455	RTA00002692F.e.10.1.P.Seq	F	M00043029C:A06	CH18CON
1587	452032	RTA00002692F.e.04.1.P.Seq	F	M00043026C:D07	CH18CON
1588	454776	RTA00002693F.f.11.2.P.Seq	F	M00043211A:F01	CH19COP
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1591	446923	RTA00002690F.d.05.3.P.Seq	F	M00042788C:F11	CH16COP
1592	449911	RTA00002691F.e.02.1.P.Seq	F	M00043384B:B02	CH17COHLV
1593	452241	RTA00002692F.c.10.2.P.Seq	F	M00042983C:G06	CH18CON
1594	452455	RTA00002692F.e.10.2.P.Seq	F	M00043029C:A06	CH18CON
1595	451052	RTA00002691F.a.10.3.P.Seq	F	M00042448A:C09	CH17COHLV
1596	450754	RTA00002691F.d.03.3.P.Seq	F	M00043366C:H05	CH17COHLV
1597	449524	RTA00002690F.a.11.3.P.Seq	F	M00042432D:E02	CH16COP
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1604	450617	RTA00002691F.e.11.1.P.Seq	F	M00043391A:G08	CH17COHLV
1605	422703	RTA00002687F.h.04.2.P.Seq	F	M00040219D:E08	CH14EDT
1606	449538	RTA00002690F.b.17.3.P.Seq	F	M00042752A:E11	CH16COP
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1616	450562	RTA00002691F.c.08.3.P.Seq	F	M00043346A:G01	CH17COHLV
1617	451196	RTA00002691F.a.23.3.P.Seq	F	M00043304B:D05	CH17COHLV
1618	446445	RTA00002689F.c.23.1.P.Seq	F	M00042717A:C07	CH15CON
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1621	448552	RTA00002690F.d.16.3.P.Seq	F	M00042807D:D05	CH16COP
1622	451559	RTA00002691F.a.11.3.P.Seq	F	M00042448C:H12	CH17COHLV
1623	377284	RTA00002683F.g.06.1.P.Seq	F	M00040060C:H10	CH09LNL
1624	449496	RTA00002690F.e.06.1.P.Seq	F	M00042830B:E02	CH16COP
1625	147196	RTA00002691F.e.20.1.P.Seq	F	M00043402C:D08	CH17COHLV
1626	373494	RTA00002690F.e.20.1.P.Seq	F	M00042852C:A01	CH16COP
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1630	451619	RTA00002691F.b.17.3.P.Seq	F	M00043324D:H11	CH17COHLV
1631	376897	RTA00002674F.l.20.2.P.Seq	F	M00039167B:H09	CH09LNL
1632	378557	RTA00002680F.i.06.2.P.Seq	F	M00039807A:D01	CH09LNL
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1636	452330	RTA00002692F.c.22.2.P.Seq	F	M00043001B:H10	CH18CON
1637	346310	RTA00002684F.d.18.2.P.Seq	F	M00040122D:A02	CH09LNL
1638	449285	RTA00002690F.e.01.2.P.Seq	F	M00042823C:C02	CH16COP
1639	377284	RTA00002683F.g.06.2.P.Seq	F	M00040060C:H10	CH09LNL
1640	377605	RTA00002683F.m.02.2.P.Seq	F	M00040089B:E04	CH09LNL
1641	378557	RTA00002680F.i.06.1.P.Seq	F	M00039807A:D01	CH09LNL
1642	403669	RTA00002687F.l.20.2.P.Seq	F	M00040326A:F04	CH14EDT
1643	447388	RTA00002689F.e.17.3.P.Seq	F	M00042905B:C03	CH15CON
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1646	447069	RTA00002689F.b.15.1.P.Seq	F	M00042567B:H10	CH15CON
1647	289519	RTA00002691F.d.18.3.P.Seq	F	M00043378A:H10	CH17COHLV
1648	32699	RTA00002713F.i.24.1.P.Seq	F	M00027475B:E10	CH04MAL
1649	373697	RTA00002678F.c.24.2.P.Seq	F	M00039454B:A11	CH09LNL

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1655	430304	RTA00002667F.k.03.1.P.Seq	F	M00032830D:G03	CH08LNH
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1663	427374	RTA00002665F.c.22.3.P.Seq	F	M00028207D:E09	CH08LNH
1664	227947	RTA00002684F.h.08.2.P.Seq	F	M00040307C:F10	CH09LNL
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1693	380354	RTA00002670F.n.23.2.P.Seq	F	M00033570B:C08	CH09LNL
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1793	80436	RTA00002661F.c.09.1.P.Seq	F	M00001582A:E02	CH01COH
1794	189139	RTA00002664F.b.14.1.P.Seq	F	M00026851B:F01	CH04MAL
1795	376614	RTA00002677F.c.05.2.P.Seq	F	M00039341D:D07	CH09LNL
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1812	428408	RTA00002665F.p.23.1.P.Seq	F	M00032513D:F01	CH08LNH
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1816	403189	RTA00002687F.g.16.2.P.Seq	F	M00040217D:B07	CH14EDT
1817	129692	RTA00002679F.e.13.1.P.Seq	F	M00039673A:F09	CH09LNL
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1820	373198	RTA00002670F.p.01.2.P.Seq	F	M00033578D:G02	CH09LNL
1821	373198	RTA00002670F.o.24.2.P.Seq	F	M00033578D:G02	CH09LNL
1822	25233	RTA00002711F.b.06.1.P.Seq	F	M00022823C:C01	CH03MAH
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1833	400097	RTA00002685F.g.19.2.P.Seq	F	M00039521A:A02	CH12EDT
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1836	429663	RTA00002667F.m.21.1.P.Seq	F	M00032864B:B09	CH08LNH
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1838	375409	RTA00002678F.n.02.2.P.Seq	F	M00039616B:C01	CH09LNL
1839	401155	RTA00002685F.o.12.2.P.Seq	F	M00039630A:C08	CH12EDT
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3	1759	RTA00002923F.f.23.1.P.Seq	F	M00039248C:A08	CH09LNL
4	10924	RTA00002907F.k.12.1.P.Seq	F	M00022224A:C07	CH03MAH
5	45331	RTA00002903F.l.10.1.P.Seq	F	M00007037D:D10	CH02COH
6	42233	RTA00002912F.g.24.1.P.Seq	F	M00027359B:A06	CH04MAL
7	7211	RTA00002909F.h.06.1.P.Seq	F	M00022634A:C07	CH03MAH
8	21395	RTA00002890F.k.16.1.P.Seq	F	M00001637D:C12	CH01COH
9	3093	RTA00002923F.e.03.1.P.Seq	F	M00039225A:D11	CH09LNL
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23	15817	RTA00002903F.o.03.1.P.Seq	F	M00007103D:C02	CH02COH
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54	23849	RTA00002887F.a.22.1.P.Seq	F	M00001386B:F11	CH01COH
55	21945	RTA00002895F.l.22.1.P.Seq	F	M00004103C:E10	CH01COH
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57	14533	RTA00002896F.l.01.1.P.Seq	F	M00004179C:B06	CH01COH
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704	186729	RTA00002911F.d.19.2.P.Seq	F	M00026850B:C09	CH04MAL
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1106	23691	RTA00002901F.g.21.1.P.Seq	F	M00005506C:E09	CH02COH
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1108	34364	RTA00002915F.o.09.2.P.Seq	F	M00032515A:B12	CH08LNH
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1154	10430	RTA00002894F.g.21.1.P.Seq	F	M00003996B:H07	CH01COH
1155	31280	RTA00002903F.k.08.1.P.Seq	F	M00007007A:E04	CH02COH
1156	19098	RTA00002925F.e.23.1.P.Seq	F	M00039861C:B12	CH09LNL
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1159	14582	RTA00002898F.d.07.1.P.Seq	F	M00004324A:D05	CH01COH
1160	21356	RTA00002917F.j.19.1.P.Seq	F	M00032753A:C07	CH08LNH
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1166	21920	RTA00002886F.j.05.1.P.Seq	F	M00001361A:C12	CH01COH
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1168	45734	RTA00002901F.j.14.1.P.Seq	F	M00005569D:G09	CH02COH
1169	12362	RTA00002929F.i.01.1.P.Seq	F	M00040391A:G05	CH14EDT
1170	9405	RTA00002892F.k.04.1.P.Seq	F	M00003830C:D02	CH01COH
1171	6507	RTA00002922F.o.05.1.P.Seq	F	M00039140A:F05	CH09LNL
1172	10735	RTA00002925F.b.24.1.P.Seq	F	M00039822A:H02	CH09LNL
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1292	32581	RTA00002932F.b.02.1.P.Seq	F	M00042986D:E03	CH18CON
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1294	1447	RTA00002935F.d.14.1.P.Seq	F	M00054536B:B01	CH17COHLV
1295	10449	RTA00002935F.o.20.1.P.Seq	F	M00055395D:D11	CH17COHLV
1296	35359	RTA00002935F.h.11.1.P.Seq	F	M00054817D:A11	CH17COHLV
1297	19657	RTA00002935F.l.20.1.P.Seq	F	M00055166C:D10	CH17COHLV
1298	12659	RTA00002930F.i.21.1.P.Seq	F	M00056133A:E11	CH15CON
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1309	16	RTA00002935F.a.06.1.P.Seq	F	M00042449B:F05	CH17COHLV
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1342	6806	RTA00002928F.d.02.1.P.Seq	F	M00040169A:G06	CH13EDT
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1344	16686	RTA00002919F.f.14.1.P.Seq	F	M00033072A:A09	CH08LNH
1345	6823	RTA00002888F.a.04.1.P.Seq	F	M00001433B:E02	CH01COH
1346	43029	RTA00002897F.d.03.1.P.Seq	F	M00004225D:E03	CH01COH
1347	14789	RTA00002935F.k.11.1.P.Seq	F	M00055055C:F01	CH17COHLV
1348	186061	RTA00002911F.f.01.1.P.Seq	F	M00026900A:H07	CH04MAL
1349	12823	RTA00002921F.g.24.1.P.Seq	F	M00033434D:F05	CH09LNL
1350	25844	RTA00002908F.k.23.1.P.Seq	F	M00022474B:C08	CH03MAH

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1354	25441	RTA00002906F.i.08.1.P.Seq	F	M00021981A:C02	CH03MAH
1355	4303	RTA00002897F.o.20.1.P.Seq	F	M00004295D:C07	CH01COH
1356	5741	RTA00002887F.c.19.1.P.Seq	F	M00001390D:E02	CH01COH
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1359	13618	RTA00002893F.o.15.1.P.Seq	F	M00003963D:F01	CH01COH
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1362	17412	RTA00002932F.b.11.1.P.Seq	F	M00043015D:D05	CH18CON
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1366	8050	RTA00002900F.n.04.1.P.Seq	F	M00005383A:C11	CH02COH
1367	186538	RTA00002929F.e.18.1.P.Seq	F	M00040329A:H05	CH14EDT
1368	25427	RTA00002935F.n.20.1.P.Seq	F	M00055337B:C04	CH17COHLV
1369	24098	RTA00002901F.a.10.1.P.Seq	F	M00005422D:H02	CH02COH
1370	123823	RTA00002905F.h.08.1.P.Seq	F	M00008071D:H03	CH03MAH
1371	3644	RTA00002901F.c.03.1.P.Seq	F	M00005445D:D04	CH02COH
1372	27783	RTA00002917F.a.17.1.P.Seq	F	M00032666A:C02	CH08LNH
1373	1682	RTA00002910F.b.03.1.P.Seq	F	M00022801D:D09	CH03MAH
1374	3200	RTA00002887F.e.07.1.P.Seq	F	M00001393C:F04	CH01COH
1375	8442	RTA00002917F.h.23.1.P.Seq	F	M00032734B:E12	CH08LNH
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1382	11315	RTA00002889F.d.12.1.P.Seq	F	M00001535B:B10	CH01COH
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1387	17156	RTA00002934F.a.08.1.P.Seq	F	M00043455B:C08	CH20COHLV
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1389	2178	RTA00002901F.m.08.1.P.Seq	F	M00005626D:G11	CH02COH
1390	1015	RTA00002933F.c.11.1.P.Seq	F	M00043213A:D05	CH19COP
1391	26792	RTA00002907F.a.18.1.P.Seq	F	M00022103C:D05	CH03MAH
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1393	14648	RTA00002898F.j.11.1.P.Seq	F	M00004365C:G11	CH01COH
1394	12585	RTA00002897F.i.20.1.P.Seq	F	M00004269A:F11	CH01COH
1395	15825	RTA00002916F.d.12.1.P.Seq	F	M00032553A:A07	CH08LNH
1396	7043	RTA00002900F.h.07.1.P.Seq	F	M00005014B:F02	CH02COH
1397	29354	RTA00002905F.c.13.1.P.Seq	F	M00007981C:F07	CH03MAH
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1404	3656	RTA00002902F.f.20.1.P.Seq	F	M00006641B:F05	CH02COH
1405	10998	RTA00002931F.c.07.1.P.Seq	F	M00042878D:G06	CH16COP
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1408	34505	RTA00002901F.a.16.1.P.Seq	F	M00005423C:A10	CH02COH
1409	8175	RTA00002924F.f.01.1.P.Seq	F	M00039472B:E05	CH09LNL
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1413	24166	RTA00002891F.k.07.1.P.Seq	F	M00003763A:B02	CH01COH
1414	15333	RTA00002888F.c.12.1.P.Seq	F	M00001442C:G12	CH01COH
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1416	9247	RTA00002930F.a.16.1.P.Seq	F	M00042560C:G06	CH15CON
1417	12317	RTA00002908F.g.13.1.P.Seq	F	M00022430C:C06	CH03MAH
1418	11968	RTA00002890F.i.24.1.P.Seq	F	M00001625D:B04	CH01COH
1419	14181	RTA00002908F.n.09.2.P.Seq	F	M00022499D:D08	CH03MAH
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1422	24898	RTA00002903F.k.17.1.P.Seq	F	M00007019B:E01	CH02COH
1423	156424	RTA00002905F.m.22.1.P.Seq	F	M00021653A:B02	CH03MAH
1424	11996	RTA00002901F.b.24.1.P.Seq	F	M00005445A:E07	CH02COH
1425	11996	RTA00002901F.c.01.1.P.Seq	F	M00005445A:E07	CH02COH
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1427	9120	RTA00002914F.h.10.1.P.Seq	F	M00028210B:H03	CH08LNH
1428	11295	RTA00002890F.j.15.1.P.Seq	F	M00001632C:A10	CH01COH
1429	3991	RTA00002896F.h.05.1.P.Seq	F	M00004162D:F02	CH01COH
1430	20358	RTA00002908F.b.06.1.P.Seq	F	M00022367D:G11	CH03MAH
1431	12823	RTA00002921F.h.01.1.P.Seq	F	M00033434D:F05	CH09LNL
1432	147419	RTA00002906F.g.05.1.P.Seq	F	M00021952B:G06	CH03MAH
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1449	2193	RTA00002933F.a.13.1.P.Seq	F	M00043077B:F11	CH19COP
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1457	4873	RTA00002930F.b.05.1.P.Seq	F	M00042719A:G08	CH15CON
1458	11214	RTA00002896F.h.01.1.P.Seq	F	M00004161A:E08	CH01COH
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1476	25620	RTA00002902F.f.09.1.P.Seq	F	M00006631C:A04	CH02COH
1477	20601	RTA00002923F.l.20.1.P.Seq	F	M00039326A:G07	CH09LNL
1478	6205	RTA00002923F.g.21.1.P.Seq	F	M00039258C:C01	CH09LNL
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1481	30321	RTA00002919F.o.17.1.P.Seq	F	M00033264B:E06	CH08LNH
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1484	5796	RTA00002908F.i.21.1.P.Seq	F	M00022457A:G05	CH03MAH
1485	3804	RTA00002935F.m.24.1.P.Seq	F	M00055254A:H03	CH17COHLV
1486	2728	RTA00002918F.a.22.1.P.Seq	F	M00032828A:A06	CH08LNH
1487	3804	RTA00002935F.n.01.1.P.Seq	F	M00055254A:H03	CH17COHLV
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1489	16691	RTA00002891F.o.03.1.P.Seq	F	M00003780A:G01	CH01COH
1490	15430	RTA00002900F.g.10.1.P.Seq	F	M00005003D:C02	CH02COH
1491	5637	RTA00002925F.b.18.1.P.Seq	F	M00039820B:F06	CH09LNL
1492	16633	RTA00002897F.g.15.1.P.Seq	F	M00004246B:H07	CH01COH
1493	21826	RTA00002898F.g.06.1.P.Seq	F	M00004344A:G11	CH01COH
1494	22193	RTA00002919F.i.09.1.P.Seq	F	M00033146D:A03	CH08LNH
1495	10720	RTA00002898F.c.14.1.P.Seq	F	M00004320C:E07	CH01COH
1496	22491	RTA00002925F.m.06.1.P.Seq	F	M00040003A:G10	CH09LNL
1497	10423	RTA00002915F.n.13.2.P.Seq	F	M00032507D:G08	CH08LNH
1498	4953	RTA00002916F.h.11.1.P.Seq	F	M00032586C:B04	CH08LNH
1499	185567	RTA00002911F.p.08.1.P.Seq	F	M00027178B:A11	CH04MAL
1500	25605	RTA00002924F.m.22.1.P.Seq	F	M00039710B:A01	CH09LNL

SEQ ID	CLUSTER	SEQ NAME	ORIENTATION	CLONE ID	LIBRARY
1501	29446	RTA00002906F.m.24.1.P.Seq	F	M00022070B:B04	CH03MAH
1502	9668	RTA00002908F.g.02.1.P.Seq	F	M00022421A:F12	CH03MAH
1503	29446	RTA00002906F.n.01.1.P.Seq	F	M00022070B:B04	CH03MAH
1504	7171	RTA00002887F.m.22.1.P.Seq	F	M00001421B:E07	CH01COH

Table 3

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
1	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
2	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
3	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
4	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
5	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
6	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
7	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
8	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
9	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
10	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
11	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
12	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
13	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
14	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
15	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
16	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
17	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
18	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
19	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
20	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
21	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
22	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>	<NONE>
23	<NONE>	<NONE>	<NONE>	548562	GENOME POLYPROTEIN [CONTAINS: RNA REPLICASE ; HELICASE: COAT PROTEIN] 2.7.7.48) - apple stem grooving virus (strain P-209)	9.2
24	<NONE>	<NONE>	<NONE>	416959	EXCISION REPAIR PROTEIN ERCC-6 DNA repair helicase ERCC6 - human >gi|182181 (L04791) excision repair protein [Homo sapiens]	8.9
25	<NONE>	<NONE>	<NONE>	3327096	(AB014541) KIAA0641 protein [Homo sapiens]	8.7
26	<NONE>	<NONE>	<NONE>	861293	(U28741) F35D2.1 gene product [Caenorhabditis elegans]	7.9
27	<NONE>	<NONE>	<NONE>	3297821	(AL031032) extensin-like protein	5.5
28	<NONE>	<NONE>	<NONE>	2119692	transforming growth factor-beta type III receptor - chicken >gi|511843 (L01121) transforming growth factor-beta type III receptor [Gallus gallus]	5.1
29	<NONE>	<NONE>	<NONE>	2136028	protein kinase PRK1 - human	5.0

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
30	<NONE>	<NONE>	<NONE>	2746912	(AF040659) No definition line found [Caenorhabditis elegans]	4.6
31	<NONE>	<NONE>	<NONE>	2358287	(AF010404) ALR [Homo sapiens]	4.5
32	<NONE>	<NONE>	<NONE>	3877816	(Z96048) predicted using Genefinder; cDNA EST EMBL:D65516 comes from this gene; cDNA EST yk191a5.5 comes from this gene [Caenorhabditis elegans]	4.4
33	<NONE>	<NONE>	<NONE>	4140268	(Y14953) SRCR domain, membrane form 2	4.1
34	<NONE>	<NONE>	<NONE>	1708663	(U51183) transposase [Hydra vulgaris]	4.0
35	<NONE>	<NONE>	<NONE>	1184100	(U45958) pistil extensin-like protein [Nicotiana alata]	3.9
36	<NONE>	<NONE>	<NONE>	121073	GLUCOCORTICOID RECEPTOR (GR)	3.9
37	<NONE>	<NONE>	<NONE>	1718298	(U75698) ORF 45; contains an extended acidic domain; EBV BKRF4 homolog [Kaposi's sarcoma-associated herpesvirus] homolog, conserved in other gamma-herpesviruses	2.6
38	<NONE>	<NONE>	<NONE>	2352538	(AF006564) alcohol dehydrogenase [Drosophila persimilis] persimilis]	1.4
39	<NONE>	<NONE>	<NONE>	3192897	(AF066071) SP85; PsB [Dictyostelium discoideum]	1.4
40	<NONE>	<NONE>	<NONE>	561645	(L33421) This CDS feature is included to show the translation of the corresponding V_region. Presently translation qualifiers on V_region features are illegal	1.0
41	<NONE>	<NONE>	<NONE>	3878857	(Z83120) predicted using Genefinder; cDNA EST EMBL:D35016 comes from this gene; cDNA EST EMBL:D32583 comes from this gene; cDNA EST EMBL:D35258 comes from this gene; cDNA EST EMBL:C11471 comes from this gene; cDNA EST EMBL:C...	1.0

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
42	<NONE>	<NONE>	<NONE>	1658571	(U75903) UGT1A7 [Rattus norvegicus]	1.0
43	<NONE>	<NONE>	<NONE>	2338034	(AF005370) putative immediate early protein [Alcelaphine herpesvirus 1]	0.86
44	<NONE>	<NONE>	<NONE>	3043714	(AB011167) KIAA0595 protein [Homo sapiens]	0.42
45	<NONE>	<NONE>	<NONE>	1723710	HYPOTHETICAL 92.7 KD PROTEIN IN ASN2-PHB1 INTERGENIC REGION >gi|2131678|pir||S64439 hypothetical protein YGR130c - yeast (Saccharomyces cerevisiae) >gi|1323215|gnl|PID|e243523 (Z72915) ORF YGR130c [Saccharomyces cerevisiae]	0.40
46	<NONE>	<NONE>	<NONE>	1723710	HYPOTHETICAL 92.7 KD PROTEIN IN ASN2-PHB1 INTERGENIC REGION >gi|2131678|pir||S64439 hypothetical protein YGR130c - yeast (Saccharomyces cerevisiae) >gi|1323215|gnl|PID|e243523 (Z72915) ORF YGR130c [Saccharomyces cerevisiae]	0.38
47	<NONE>	<NONE>	<NONE>	2996117	(AF046125) immediate early 2 [Rat cytomegalovirus]	0.26
48	<NONE>	<NONE>	<NONE>	4151809	(AF102855) synaptic SAPAP-interacting protein Synamon	0.024
49	<NONE>	<NONE>	<NONE>	2773341	(AF040954) putative protein phosphatase 1 nuclear targeting subunit [Rattus norvegicus]	0.017
50	<NONE>	<NONE>	<NONE>	1653522	(D90914) hypothetical protein	3e-04
51	<NONE>	<NONE>	<NONE>	3219965	HYPOTHETICAL 100.6 KD TRP-ASP REPEATS CONTAINING PROTEIN C2C6.04C IN CHROMOSOME I	3e-06
52	<NONE>	<NONE>	<NONE>	4185567	(AF115480) cAMP-dependent Rap1 guanine-nucleotide exchange factor [Mus musculus]	7e-07

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
53	<NONE>	<NONE>	<NONE>	1176527	HYPOTHETICAL 43.2 KD PROTEIN C34E10.1 IN CHROMOSOME III >gi|500724 (U10402) C34E10.1 gene product [Caenorhabditis elegans]	3e-20
54	X85444	G.pallida repetitive DNA element	5.0	2118936	beta-globin - chimpanzee (fragment)	8.6
55	X72961	Synechococcus sp. cpeB, cpeA genes and ORF3	5.0	462569	MICROTUBULE-ASSOCIATED PROTEIN 1A microtubule-associated protein MAP1A - rat >gi|205538 norvegicus]	2.2
56	U94747	Human WD repeat protein HAN11 mRNA, complete cds	5.0	3875538	(Z67990) similar to cuticle collagen	1.3
57	AF032108	Homo sapiens integrin alpha-7 mRNA, complete cds	5.0	2147194	collagen - Paralvinella grasslei	0.002
58	Z50798	G.gallus mRNA for p52	5.0	3122885	ASPARTYL-TRNA SYNTHETASE synthetase [Bacillus subtilis]	3e-11
59	AB002384	Human mRNA for KIAA0386 gene, complete cds	5.0	2632098	(Y15513) Prodos protein [Drosophila melanogaster]	9e-12
60	X14835	Thermofilum pendens DNA for 16S and 23S ribosomal RNA, tRNA-Met, and tRNA Gly	4.9	<NONE>	<NONE>	<NONE>
61	U87149	Hordeum vulgare nucellin gene, complete cds	4.9	128578	NONSTRUCTURAL PROTEIN NS-S spotted wilt virus (strain CPNH1) non-structural protein [Tomato spotted wilt virus]	2.8
62	D87541	Mus musculus gene for integrin alpha v subunit, promoter region	4.9	136956	HYPOTHETICAL PROTEIN UL61 cytomegalovirus (strain AD169) cytomegalovirus]	0.038
63	U72520	Mus musculus mena protein (Mena) mRNA, complete cds	4.9	3413892	(AB007934) KIAA0465 protein [Homo sapiens]	6e-07

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
64	S79797	enzymatic glycosylation-regulating gene [rats, Sprague-Dawley, streptozotocin diabetic, heart, mRNA, 5010 nt]	4.8	<NONE>	<NONE>	<NONE>
65	AB011102	Homo sapiens mRNA for KIAA0530 protein, partial cds	4.8	138022	RECEPTOR RECOGNIZING PROTEIN gp38 - phage Ox2 >gi|15126 (X05675) gene 38 (AA 1-266); pid:g15126 [Bacteriophage Ox2]	3.6
66	AF100985	Penaeus monodon phosphopyruvate hydratase mRNA, complete cds	4.8	500615	(D16221) endochitinase [Oryza sativa]	2.8
67	U31756	Bacillus subtilis gamma-aminobutyrate permease cds	4.8	3880699	(AL021471) similar to Eukaryotic aspartyl proteases [Caenorhabditis elegans] Eukaryotic aspartyl proteases [Caenorhabditis elegans]	2.8
68	U25111	Pisum sativum chloroplast processing enzyme mRNA, nuclear gene encoding chloroplast protein, complete cds.	4.8	1800145	(U83658) FH1/FH2 protein homolog [Emericella nidulans]	1.6
69	U00454	Mus musculus Cdx-2 homeobox protein gene, complete cds.	4.7	<NONE>	<NONE>	<NONE>
70	M84166	Hamster c-Ha-ras protein gene, complete cds.	4.7	1710606	RENIN-BINDING PROTEIN (RNBP) protein [Rattus norvegicus]	0.88
71	AF087516	Mus musculus major sperm fibrous sheath protein Pro-mAKAP82 gene, alternative splice exons 1' and 1"	4.6	<NONE>	<NONE>	<NONE>
72	X74160	M.esculenta mRNA for granule-bound starch synthase	4.6	<NONE>	<NONE>	<NONE>
73	M97487	Haloferax volcanii superoxide dismutase (sod2) gene, complete cds.	4.6	2623307	(AC002409) putative ubiquitin protease [Arabidopsis thaliana]	3.4

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
74	M57889	Drosophila melanogaster suppressor of sable gene, complete cds.	4.5	<NONE>	<NONE>	<NONE>
75	D49708	Rattus norvegicus mRNA for RNA binding protein	4.5	<NONE>	<NONE>	<NONE>
76	D31853	Yeast GTS1 gene for glycin-threonin/serine repeat protein, complete cds	4.5	2447195	(U42580) NETTF (7x), DETTS (4x) [Paramecium bursaria Chlorella virus 1]	3.3
77	Z47036	Human partial cDNA sequence, clone bs613;	2.9	<NONE>	<NONE>	<NONE>
78	L19660	Rattus norvegicus gastric inhibitory peptide receptor mRNA, complete cds	2.7	2358279	(AF007871) torsinA [Homo sapiens]	2e-07
79	X82841	A.thaliana Aco gene	2.6	483212	immediate-early protein IE110 - human herpesvirus 1 (strain HFEM) (fragment)	8.4
80	X61931	S.purpurascens famA and famB genes for FAS domain and acyl-CoA-dehydrogenases, respectively	2.6	2290534	(U95031) sublingual gland mucin [Homo sapiens]	0.47
81	U13680	Human lactate dehydrogenase-C (LDH-C) mRNA, complete cds.	2.5	2887449	(AB007874) KIAA0414 [Homo sapiens]	3.1
82	AB007869	Homo sapiens KIAA0409 mRNA, partial cds	2.4	3130157	(AB008859) pheromone receptor [Fugu rubripes]	5.4
83	X97479	H.sapiens mas proto-oncogene, 5' region	2.1	<NONE>	<NONE>	<NONE>
84	X98374	R.norvegicus mRNA for KIS protein	1.9	<NONE>	<NONE>	<NONE>
85	AE000710	Aquifex aeolicus section 42 of 109 of the complete genome	1.9	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
86	D30612	Homo sapiens mRNA for repressor protein, partial cds	1.9	<NONE>	<NONE>	<NONE>
87	Y14321	Homo sapiens PMP69 gene, exons 8,9,10 & 11	1.9	<NONE>	<NONE>	<NONE>
88	D90773	E.coli genomic DNA, Kohara clone #262(30.3-30.5 min.)	1.9	1536816	(D78305) DNA binding protein [Chlorella virus]	7.9
89	AE000991	Archaeoglobus fulgidus section 116 of 172 of the complete genome	1.9	520645	(X79095) pyruvate,orthophosphate dikinase [Flaveria trinervia]	2.7
90	U39476	Rattus norvegicus p95 Vav (Vav) proto-oncogene mRNA, complete cds.	1.9	4158178	(AL023496) hypothetical protein	1.6
91	U28838	Human transcription factor TFIIIB 90 kDa subunit	1.9	2495730	HYPOTHETICAL PROLINE-RICH PROTEIN KIAA0269 >gi|1665805|gnl|PID|d1014089 (D87459) Similar to Volbox carteri extensin (S22697) [Homo sapiens]	0.23
92	U20106	Rattus norvegicus synaptotagmin VII mRNA, complete cds.	1.9	478380	UL47h protein - Marek's disease virus	0.23
93	AF071010	Mouse mammary tumor virus putative integrase, env polyprotein, and superantigen mRNA, complete cds	1.9	2781386	(AC004010) similar to Leucine-rich transmembrane proteins; 44% similarity to U42767 (PID:g1736918) [Homo sapiens]	4e-33
94	AF061881	Mesocricetus auratus c-fos proto-oncogene protein (c-fos) gene, complete cds	1.8	<NONE>	<NONE>	<NONE>
95	AE001397	Plasmodium falciparum chromosome 2, section 34 of 73 of the complete sequence	1.8	<NONE>	<NONE>	<NONE>

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
96	D14701	Horseshoe crab mRNA for coagulation factor B, complete cds	1.8	<NONE>	<NONE>	<NONE>
97	M29154	P.falciparum multidrug resistance (MDR) gene, complete cds.	1.8	<NONE>	<NONE>	<NONE>
98	L16532	Rattus norvegicus (clone pCNPII) 2',3'-cyclic nucleotide 3'-phosphodiesterase (CNPII) mRNA, complete cds.	1.8	<NONE>	<NONE>	<NONE>
99	AE001434	Plasmodium falciparum chromosome 2, section 71 of 73 of the complete sequence	1.8	<NONE>	<NONE>	<NONE>
100	Z46785	D.melanogaster gene for protamine (mst35Bb).	1.8	<NONE>	<NONE>	<NONE>
101	X69822	P.sylvestris mRNA for glutamine synthetase	1.8	219896	(D90452) l-caldesmon I [Homo sapiens]	9.7
102	U49055	Rattus norvegicus CTD-binding SR-like protein rA8 mRNA, complete cds	1.8	2497252	INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN 4 (IGFBP-4) (IBP-4) (IGF-BINDING PROTEIN 4) factor-binding protein-4 - sheep (fragment) factor-binding protein-4, IGFBP-4 [sheep, liver, Peptide, 237 aa] [Ovis aries]	2.5
103	L28101	Homo sapiens kallistatin (PI4) gene, exons 1-4, complete cds	1.8	4204267	(AC005223) 55585 [Arabidopsis thaliana]	2.4
104	U66987	Pandorina morum internal transcribed spacer 1, 5.8S ribosomal RNA gene, and internal transcribed spacer 2, complete sequence	1.8	2635909	(Z99121) permease [Bacillus subtilis]	1.9

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
105	X58033	Human polymorphic MspI site DNA (D3S3 locus)	1.8	2136878	keratin KAP5.5 - sheep (fragment) >gi|313722	0.65
106	U15780	Human p82 (ST5) mRNA, alternatively spliced, complete cds	1.8	3638957	(AC004877) sco-spondin-mucin-like; similar to P98167 uncertain [Homo sapiens]	0.64
107	AF038535	Homo sapiens synaptotagmin VII mRNA, partial cds	1.8	457927	(U00690) calcium channel alpha-1 subunit [Drosophila melanogaster]	0.51
108	AF052134	Homo sapiens clone 23585 mRNA sequence	1.8	232263	HOMEOBOX PROTEIN HOX-D1 (HOX-4.9)	0.28
109	X75208	H.sapiens HEK2 mRNA for protein tyrosine kinase receptor.	1.8	1730198	GROWTH-ARREST-SPECIFIC PROTEIN 1 gene product [Homo sapiens]	0.22
110	AB013896	Xenopus laevis mRNA for SOX-D, complete cds	1.8	2494501	TRANSCRIPTION FACTOR FKH-4 factor [Mus musculus]	0.17
111	D16947	Human HepG2 3' region cDNA, clone hmd6b10	1.8	3413870	(AB007923) KIAA0454 protein [Homo sapiens]	0.002
112	D13547	Mouse DNA, T early alpha (TEA) region	1.8	3393018	(AL031174) hypothetical protein	5e-08
113	M35498	Woodchuck c-myc protein gene, exon 1.	1.8	3183405	HYPOTHETICAL 11.3 KD PROTEIN C2C6.07 IN CHROMOSOME I >gi|2370504|gnl|PID|e339194 pombe] >gi|3451305|gnl|PID|e1316730 (AL031324) very hypothetical protein [Schizosaccharomyces pombe]	8e-10
114	M84166	Hamster c-Ha-ras protein gene, complete cds.	1.8	3386622	(AC004665) unknown protein [Arabidopsis thaliana]	2e-10
115	U33135	Mychodea carnosa 18S ribosomal RNA gene, complete sequence	1.8	3334982	(AC005306) R27216_1 [Homo sapiens]	3e-22
116	U84003	Homo sapiens putative tumor suppressor (BIN1) gene, exons 7-12	1.7	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
117	AE001121	Borrelia burgdorferi (section 7 of 70) of the complete genome	1.7	<NONE>	<NONE>	<NONE>
118	AE001114	Archaeoglobus fulgidus section 165 of 172 of the complete genome	1.7	<NONE>	<NONE>	<NONE>
119	U82064	Angiostrongylus cantonensis adult-specific muscle protein-1 gene, partial cds	1.7	<NONE>	<NONE>	<NONE>
120	AF041836	Buchnera aphidicola plasmid pLeu-Sg, complete plasmid sequence	1.7	<NONE>	<NONE>	<NONE>
121	M87479	Lymnaea stagnalis FMRFamide gene, mature peptides.	1.7	<NONE>	<NONE>	<NONE>
122	M55163	Xenopus laevis fibroblast growth factor receptor mRNA, complete cds.	1.7	<NONE>	<NONE>	<NONE>
123	S57565	histamine H2-receptor [rats, Genomic, 1928 nt]	1.7	<NONE>	<NONE>	<NONE>
124	M27256	Simian immunodeficiency virus (SIV) pol region.	1.7	<NONE>	<NONE>	<NONE>
125	U31516	Human chromosome 8 anonymous clone pBS8-165	1.7	<NONE>	<NONE>	<NONE>
126	X12671	Human gene for heterogeneous nuclear ribonucleoprotein (hnRNP) core protein A1	1.7	<NONE>	<NONE>	<NONE>
127	AF009054	Paeonia suffruticosa ssp. spontanea alcohol dehydrogenase 1B (Adh1B) gene, partial cds	1.7	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
128	AF046917	Mus musculus transketolase gene, exon 6 and partial cds	1.7	<NONE>	<NONE>	<NONE>
129	D89053	Homo sapiens mRNA for Acyl-CoA synthetase 3, complete cds	1.7	<NONE>	<NONE>	<NONE>
130	U57968	Staphylothermus marinus surface layer-associated STABLE protease gene, complete cds.	1.7	<NONE>	<NONE>	<NONE>
131	L39072	Bovine herpesvirus 1 (clone p95) UL24 homologue gene, complete cds.	1.7	<NONE>	<NONE>	<NONE>
132	X04980	Drosophila simulans retrotransposon 297 5'-LTR and flanks (pWK1020)	1.7	<NONE>	<NONE>	<NONE>
133	AE001114	Archaeoglobus fulgidus section 165 of 172 of the complete genome	1.7	<NONE>	<NONE>	<NONE>
134	X04434	Human mRNA for insulin-like growth factor I receptor	1.7	<NONE>	<NONE>	<NONE>
135	U07890	Mus musculus C57BL/6J epidermal surface antigen (mesa) mRNA, complete cds.	1.7	<NONE>	<NONE>	<NONE>
136	D26163	Human tyrosinase gene, 5'-flanking region cell-specific transcription)	1.7	<NONE>	<NONE>	<NONE>
137	AF093818	Panorpa nipponensis NADH dehydrogenase subunit 5 gene, mitochondrial gene encoding mitochondrial protein, partial cds	1.7	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		Xenopus laevis				
138	D50560	mRNA for cytochrome P-450, complete cds	1.7	<NONE>	<NONE>	<NONE>
139	AF083488	Mus musculus phospholipase D1 (PLD1) gene, exons 18 and 19, complete sequence	1.7	<NONE>	<NONE>	<NONE>
140	AF100694	Mus musculus Pontin52 mRNA, complete cds	1.7	<NONE>	<NONE>	<NONE>
141	M73749	Streptococcus salivarius thermophilus beta-D-galactose (lacZ) gene, complete cds. > :: gb|M63636|STRLACZZ Streptococcus thermophilus beta-D-galactosidase (lacZ) gene, complete cds.	1.7	<NONE>	<NONE>	<NONE>
142	AE001114	Archaeoglobus fulgidus section 165 of 172 of the complete genome	1.7	2183023	(U84971) unknown [Homo sapiens]	9.2
143	L01983	Human type IV sodium channel alpha polypeptide	1.7	130504	GENOME POLYPROTEIN [CONTAINS: N-TERMINAL PROTEIN (P1); HELPER COMPONENT PROTEINASE INCLUSION PROTEIN (CI); 6 KD PROTEIN 2 (6K2); GENOME-LINKED PROTEIN (VPG); NUCLEAR ... virus (strain D)	9.2
144	L19731	Plecotus rafinesquii mitochondrial cytochrome b gene, 5' end.	1.7	3327096	(AB014541) KIAA0641 protein [Homo sapiens]	9.1
145	AE001114	Archaeoglobus fulgidus section 165 of 172 of the complete genome	1.7	2183023	(U84971) unknown [Homo sapiens]	8.8

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
146	L27218	Bos taurus serum amine oxidase mRNA, complete cds. > oxidase=amiloride-binding protein homolog [cattle, liver, mRNA, 2664 nt]	1.7	1174459	SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION 6 (IL-4 STAT) >gi|559855 (U16031) IL-4 Stat [Homo sapiens]	7.1
147	Z49868	Caenorhabditis elegans cosmid W07E11, complete sequence [Caenorhabditis elegans]	1.7	4204263	(AC005223) 40409 [Arabidopsis thaliana]	6.7
148	AL022271	Caenorhabditis elegans cosmid F32F2, complete sequence [Caenorhabditis elegans]	1.7	2497969	PERIPLASMIC NITRATE REDUCTASE PRECURSOR >gi|1086107|pir||S50163 nitrate reductase large chain precursor, periplasmic - Thiosphaera pantotropha >gi|600093 (Z36773) periplasmic nitrate reductase large subunit [Paracoccus denitrificans]	6.7
149	U43844	Mus musculus cyclin D3 gene, complete cds	1.7	3861490	(AF062037) capsid protein precursor [Thosea asigna virus]	5.1
150	Z25464	S.cerevisiae UNF1, LTV1, MRP8, CYB3 and TGL1 genes, complete CDS's	1.7	1255404	(U53151) weak similarity to cytochrome b [Caenorhabditis elegans]	4.1
151	U77846	Human elastin gene, partial cds and partial 3'UTR	1.7	3355682	(AL031124) putative secreted lyase	4.0
152	X62880	S.scrofa mRNA for calcium release channel (CRC)	1.7	3327080	(AB014533) KIAA0633 protein [Homo sapiens]	4.0
153	Y00067	Human gene for neurofilament subunit M (NF-M)	1.7	479829	heterogeneous ribonuclear particel protein homolog - Caenorhabditis elegans similarity to RNA recognition motifs [Caenorhabditis elegans]	3.9

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
154	X68393	D.melanogaster gene for Beta-tubulin, exons 1 and 2	1.7	2342682	(AC000106) Contains similarity to Rattus AMP-activated protein kinase (gb|X95577). [Arabidopsis thaliana]	3.8
155	AB012284	Shuttle vector pAUR123 gene for Aur1-C, complete cds	1.7	417704	POL POLYPROTEIN (ORF1A/1B) [CONTAINS: RNA-DIRECTED RNA POLYMERASE : HELICASE; PROTEASE]	3.8
156	M96633	Rattus norvegicus mitochondrial intermediate peptidase (MIP) mRNA, complete cds.	1.7	2314209	(AE000613) H. pylori predicted coding region HP1054	3.1
157	U49055	Rattus norvegicus CTD-binding SR-like protein rA8 mRNA, complete cds	1.7	2497252	INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN 4 (IGFBP-4) (IBP-4) (IGF-BINDING PROTEIN 4) factor-binding protein-4 - sheep (fragment) factor-binding protein-4, IGFBP-4 [sheep, liver, Peptide, 237 aa] [Ovis aries]	3.0
158	Y15907	Mus musculus mRNA for myc-intron-binding protein-1	1.7	912776	iduronate-2-sulfatase, IDS {EC 3.1.6.13} Peptide Mutant, 550 aa]	3.0
159	U67600	Methanococcus jannaschii section 142 of 150 of the complete genome	1.7	2982355	(AF052252) fork head domain protein FKD9 [Danio rerio]	3.0
160	AF013759	Homo sapiens calumein (Calu) mRNA, complete cds	1.7	2982355	(AF052252) fork head domain protein FKD9 [Danio rerio]	2.9

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
161	AF062915	Arabidopsis thaliana putative transcription factor (MYB90) mRNA, complete cds	1.7	3878065	(AL021666) Similarity to Human mRNA product KIAA0077 (TR:Q14997); cDNA EST yk243h8.5 comes from this gene; cDNA EST yk243h8.3 comes from this gene; cDNA EST yk359h4.5 comes from this gene [Caenorhabditis elegans] >gi|3880318|gnl|PID|e1349839 (Z81133) Similarity to Human mRNA product KIAA0077 (TR:Q14997); cDNA EST yk243h8.5 comes from this gene; cDNA EST yk243h8.3 comes from this gene; cDNA EST yk359h4.5 comes from this gene	2.3
162	X87526	H.sapiens genomic DNA (chromosome 3; clone NL3003R)	1.7	3638957	(AC004877) sco-spondin-mucin-like; similar to P98167 uncertain [Homo sapiens]	2.3
163	AC005573	Homo sapiens chromosome 5, PAC clone 202e13	1.7	2465540	(AF005632) phosphodiesterase I/nucleotide pyrophosphatase beta [Homo sapiens]	1.8
164	D83402	Homo sapiens gene for prostacyclin synthase, exon 10 and complete cds	1.7	627608	steroid hormone receptor TR3 - human sapiens]	1.7
165	AF053700	Homo sapiens deltex (Dx) mRNA, complete cds	1.7	2662089	(AB007864) KIAA0404 [Homo sapiens]	1.7
166	AF043225	Mus musculus 6-pyruvoyl-tetrahydropterin synthase (Pts) mRNA, complete cds	1.7	2352538	(AF006564) alcohol dehydrogenase [Drosophila persimilis] persimilis]	1.4

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
167	U52917	Thermus aquaticus thermophilus NADH dehydrogenase I subunits NQO7 NQO6, NQO5, NQO4, NQO2, NQO1, NQO3, NQO8, NQO9, NQO10, NQO11, NQO12, NQO13, and NQO14, complete cds.	1.7	2564334	(AB006631) The human homolog of mouse Cux-2 [Homo sapiens]	1.0
168	X72222	M.musculus gene for serotonin 2 receptor	1.7	3875796	(Z73425) Similarity to Yeast hypothetical YIK9 protein (SW:YIK9_YEAST); cDNA EST EMBL:T01252 comes from this gene; cDNA EST EMBL:D33205 comes from this gene; cDNA EST EMBL:D33955 comes from this gene; cDNA EST EMBL:D35484 co...	1.0
169	U23186	Crotalus scutulatus PLA2-like pseudogene	1.7	853971	(X83413) DR5 [Human herpesvirus 6] >gi|853972 (X83413) DR5 [Human herpesvirus 6]	0.99
170	M83118	Mus musculus factor VIII-associated protein (f8a) mRNA, complete cds.	1.7	3201617	(AC004669) hypothetical protein [Arabidopsis thaliana]	0.80
171	M38347	E.coli ATP-dependent proteinase (lon) gene, complete cds.	1.7	4140322	(AL031282) dJ283E3.3.2 (Cell Division Cycle 2-Like 2 (PITSLRE, p58/GTA, Galactosyltransferase Associated Protein Kinase)) (isoform beta 2-2) [Homo sapiens]	0.78
172	U28838	Human transcription factor TFIIIB 90 kDa subunit	1.7	2495730	HYPOTHETICAL PROLINE-RICH PROTEIN KIAA0269 >gi|1665805|gnl|PID|d1014089 (D87459) Similar to Volbox carteri extensin (S22697) [Homo sapiens]	0.62

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
173	U72487	Rattus norvegicus calcium-independent alpha-latrotoxin receptor mRNA, complete cds	1.7	544411	GLYCOPROTEIN GP100 PRECURSOR (P29F8) discoideum]	0.35
174	AE000718	Aquifex aeolicus section 50 of 109 of the complete genome	1.7	2497569	FIBROBLAST GROWTH FACTOR RECEPTOR 3 PRECURSOR (FGFR-3) (HEPARIN-BINDING GROWTH FACTOR RECEPTOR) >gi|2117851|pir||I55363 fibroblast growth factor receptor 3 - mouse >gi|199145 (M81342) fibroblast growth factor receptor 3 [Mus musculus]	0.34
175	AF016897	Oryza sativa GDP dissociation inhibitor protein OsGDI2 (OsGDI2) mRNA, complete cds	1.7	125362	MACROPHAGE COLONY STIMULATING FACTOR I RECEPTOR PRECURSOR (CSF-1-R) (FMS PROTO-ONCOGENE) (C-FMS) factor 1 receptor - cat >gi|163855 (J03149) M-CSF receptor [Felis domesticus]	0.34
176	U95102	Xenopus laevis mitotic phosphoprotein 90 mRNA, complete cds	1.7	85058	muscarinic acetylcholine receptor - fruit fly acetylcholine receptor [Drosophila melanogaster]	0.20
177	AF077352	Chlamydomonas reinhardtii myosin heavy chain	1.7	728901	ACROSOMAL PROTEIN SP-10 PRECURSOR SP-10 - western baboon >gi|298488|bbs|127113 (S56458) SP-10=intraacrosomal protein [Papio papio=baboons, Peptide, 285 aa] [Papio hamadryas]	0.20
178	Z92788	Caenorhabditis elegans cosmid F53B8, complete sequence [Caenorhabditis elegans]	1.7	746516	(U23517) D1022.7 [Caenorhabditis elegans] >gi|3258651 elegans]	0.068

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
179	AF002217	Ralstonia eutropha megaplasmid pHG1 nitric oxide reductase (norB) gene, complete cds	1.7	1143538	(X87883) mitochondrial capsule selenoprotein [Rattus norvegicus] >gi|1354135 (U48702) mitochondia associated cysteine-rich protein SMCP	0.039
180	D30749	Rat mRNA for protein tyrosine phosphatase	1.7	1228035	(D83776) The KIAA0191 gene is expressed ubiquitously.; The KIAA0191 protein retains the C2H2 zinc-finger at its N-terminal region. [Homo sapiens]	0.008
181	M15202	Rat fast skeletal TnT gene encoding troponin T isoforms, complete cds.	1.7	731172	SKIN SECRETORY PROTEIN XP2 PRECURSOR	4e-04
182	L07592	Human peroxisome proliferator activated receptor mRNA, complete cds.	1.7	4033414	PUTATIVE IMPORTIN BETA-4 SUBUNIT	2e-06
183	U64031	Dendrobium crumenatum ACC synthase gene, complete cds	1.7	3122885	ASPARTYL-TRNA SYNTHETASE synthetase [Bacillus subtilis]	2e-11
184	AF034970	Homo sapiens docking protein (DOK-2) mRNA, complete cds	1.7	2289097	(U78737) alpha(1,3)fucosyltransferase [Cricetulus griseus]	8e-12
185	Z12839	L.longiflorum mRNA encoding calmodulin. > :: gb|L18912|LILCALMODU Lilium longiflorum calmodulin mRNA, complete cds.	1.7	2511747	(AF023270) probable transcriptional regulator dre4	4e-12

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
186	X53459	Equine arteritis virus (EAV) RNA genome > :: emb|A45589|A45589 Sequence 1 from Patent WO9519438 > :: emb|A58849|A58849 Sequence 1 from Patent WO9700963 > :: gb|AR013959|AR013959 Sequence 1 from patent US 5773235	1.7	3979817	(Z70683) Weak similarity to Human tyrosine-protein kinase CSK (SW:CSK_HUMAN); cDNA EST EMBL:C10908 comes from this gene; cDNA EST EMBL:C12822 comes from this gene; cDNA EST yk408c2.3 comes from this gene; cDNA EST yk408c2.5 ... Human tyrosine-protein kinase CSK (SW:CSK_HUMAN); cDNA EST EMBL:C10908 comes from this gene; cDNA EST EMBL:C12822 comes from this gene; cDNA EST yk408c2.3 comes from this gene; cDNA EST yk408c2.5 ...	1e-14
187	K02668	E. coli ddl gene encoding D-alanine:D-alanine ligase and ftsQ and ftsA genes, complete cds, and ftsZ gene, 5' end.	1.7	3879121	(Z70310) predicted using Genefinder; Similarity to Mouse ankyrin (PIR Acc. No. S37771); cDNA EST EMBL:T01923 comes from this gene; cDNA EST EMBL:D32335 comes from this gene; cDNA EST EMBL:D32723 comes from this gene; cDNA ES... Genefinder; Similarity to Mouse ankyrin (PIR Acc. No. S37771); cDNA EST EMBL:T01923 comes from this gene; cDNA EST EMBL:D32335 comes from this gene; cDNA EST EMBL:D32723 comes from this gene; cDNA ES...	2e-19
188	AB008375	Homo sapiens mRNA for osteoblast specific cysteine-rich protein, complete cds	1.7	2496945	HYPOTHETICAL 55.9 KD PROTEIN EEED8.6 IN CHROMOSOME II >gi|733603 (U23484) No definition line found [Caenorhabditis elegans]	1e-19
189	L36603	Pseudomonas cepacia (clone Psudom70-1) heat shock protein 70 (hsp70) gene, complete cds	1.7	2661842	(Y15732) DNA polymerase beta [Xenopus laevis]	6e-20

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
190	Z49760	P.blakesleeanus mRNA GTP cyclohydrolase I	1.7	1731181	HYPOTHETICAL 75.5 KD PROTEIN C14A4.3 IN CHROMOSOME II >gi|3874230|gnl|PID|e1351618 protein (Swiss Prot accession number P38376); cDNA EST yk220e10.5 comes from this gene [Caenorhabditis elegans]	3e-21
191	U52428	Human fatty acid synthase gene, partial cds	1.7	4226073	(AF125443) contains similarity to S. pombe phosphatidyl synthase (GB:Z28295) [Caenorhabditis elegans]	6e-25
192	U12767	Human mitogen induced nuclear orphan receptor	1.6	<NONE>	<NONE>	<NONE>
193	Z63478	H.sapiens CpG DNA, clone 85a12, forward read cpg85a12.ft1a .	1.6	<NONE>	<NONE>	<NONE>
194	AF084375	Homo sapiens inversin protein, exons 8 and 9	1.6	<NONE>	<NONE>	<NONE>
195	AE001114	Archaeoglobus fulgidus section 165 of 172 of the complete genome	1.6	<NONE>	<NONE>	<NONE>
196	AF084375	Homo sapiens inversin protein, exons 8 and 9	1.6	<NONE>	<NONE>	<NONE>
197	U24217	Kluyveromyces lactis RNA polymerase II largest subunit gene, partial cds	1.6	<NONE>	<NONE>	<NONE>
198	AE000580	Helicobacter pylori 26695 section 58 of 134 of the complete genome	1.6	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
199	X62083	H.sapiens mRNA for Drosophila female sterile homeotic (FSH) homologue > :: gb|M80613|HUMFS HG Human homolog of Drosophila female sterile homeotic mRNA, complete cds.	1.6	<NONE>	<NONE>	<NONE>
200	M28064	Plasmodium brasilianum DNA homologous to the histidine-rich knob protein region of Plasmodium falciparum.	1.6	457495	(M26647) ORF X [Saccharomyces cerevisiae]	8.4
201	U03114	Streptomyces albus lipase precursor (lip) gene, complete cds, and unidentified 5' ORF and 3' ORF, partial cds.	1.6	3638957	(AC004877) sco-spondin-mucin-like; similar to P98167 uncertain [Homo sapiens]	7.8
202	U88422	Strix varia oocyte maturation factor Mos (c-mos) proto-oncogene, partial cds	1.6	137618	VITAMIN D3 RECEPTOR (VDR) receptor [Rattus norvegicus]	6.4
203	M68519	Human pulmonary surfactant-associated protein SP-A (SFTP1) gene, complete cds.	1.6	3875423	(Z38112) E03A3.6 [Caenorhabditis elegans]	4.9
204	AF044575	Homo sapiens transcription factor POU4F3	1.6	2133625	GABA transport protein - tobacco hornworm	4.7
205	L48476	Homo sapiens (subclone 3_e10 from P1 H21) DNA sequence.	1.6	3687297	(AJ005588) 5-epi-aristolochene synthase	4.6
206	M18630	Rat CNS 2',3'-cyclic nucleotide 3-phosphodiesterase	1.6	3880315	(Z81133) Similarity to Human mRNA product KIAA0077 (TR:Q14997) [Caenorhabditis elegans]	3.7

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
207	AF027174	Arabidopsis thaliana cellulose synthase catalytic subunit (Ath-B) mRNA, complete cds	1.6	267068	TUMOR-ASSOCIATED ANTIGEN L6	3.6
208	U53448	Babesia microti heat shock protein 70 (hsp70) gene, complete cds	1.6	1255429	(U53155) strong similarity to the carboxyl two-thirds of valyl-tRNA synthetases [Caenorhabditis elegans]	2.2
209	AF084367	Homo sapiens inversin protein mRNA, complete cds	1.6	1730076	PROBABLE SERINE/THREONINE-PROTEIN KINASE CY49.28 >gi|1370255|gnl|PID|e247094 (Z73966) pknJ	1.2
210	D55635	Yeast dis1+ gene for p93dis1, complete cds	1.6	3128353	(AF010496) maltose transport inner membrane protein	1.2
211	AF035756	Streptomyces sp. 2-dehydro-3-deoxyphosphohepton ate aldolase gene, partial cds	1.6	853971	(X83413) DR5 [Human herpesvirus 6] >gi|853972 (X83413) DR5 [Human herpesvirus 6]	0.97
212	X73479	O.cuniculus rPTPA mRNA	1.6	3413810	(Y17034) Bassoon [Mus musculus]	0.94
213	X98330	H.sapiens mRNA for ryanodine receptor 2	1.6	2072986	(U95142) putative G-protein-coupled receptor G-protein-coupled receptor [Arabidopsis thaliana]	0.73
214	X64194	P.anserina FMR1 gene exons 1 and 2	1.6	128014	NECDIN >gi|91129|pir||JN0148 necdin, brain - mouse >gi|200020 (M80840) necdin [Mus musculus]	0.42
215	Z92788	Caenorhabditis elegans cosmid F53B8, complete sequence [Caenorhabditis elegans]	1.6	746516	(U23517) D1022.7 [Caenorhabditis elegans] >gi|3258651 elegans]	0.19
216	AE000888	Methanobacterium thermoautotrophicum from bases 1098908 to 1112186 (section 94 of 148) of the complete genome	1.6	462415	INTERFERON-ALPHA/BETA RECEPTOR ALPHA CHAIN PRECURSOR (IFN-ALPHA-REC) >gi|346520|pir||S27387 interferon alpha receptor type 1 - bovine >gi|432	0.001

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
217	AB008375	Homo sapiens mRNA for osteoblast specific cysteine-rich protein, complete cds	1.6	2496945	HYPOTHETICAL 55.9 KD PROTEIN EEED8.6 IN CHROMOSOME II >gi|733603 (U23484) No definition line found [Caenorhabditis elegans]	1e-18
218	M25312	Orang-utan involucrin gene, complete cds.	1.6	3875131	(Z70750) similar to vanadate resistance protein transmembranous domains [Caenorhabditis elegans]	3e-26
219	AB012882	Cyprinus carpio mRNA for MyoD, complete cds	1.5	<NONE>	<NONE>	<NONE>
220	U29487	Caenorhabditis elegans cosmid C09C7	1.5	<NONE>	<NONE>	<NONE>
221	X74760	M.musculus mRNA for Notch 3	1.5	1364094	integral membrane protein - Streptomyces pristinaespiralis >gi|872306 (X84072) integral membrane protein [Streptomyces pristinaespiralis]	4.3
222	U72396	Lycopersicon esculentum class II small heat shock protein Le-HSP17.6 mRNA, complete cds	1.5	121855	EXOGLUCANASE II PRECURSOR cellulose 1,4-beta cellobiosidase (EC 3.2.1.91) II precursor - fungus (Trichoderma reesei) 1,4-beta-cellobiosidase (EC 3.2.1.91) II - fungus cellobiohydrolase II [Trichoderma reesei]	4.3
223	U42391	Human myosin-IXb mRNA, complete cds	1.5	3688428	(AJ011534) sucrose synthase	4.2
224	M92296	Pongo pygmaeus gamma-1 and gamma-2 globin genes, complete cds.	1.5	186413	(M13144) inhibin A [Homo sapiens]	0.22
225	X94144	C.japonica mRNA for QNR-71 protein	1.5	2745737	(AF029791) UDP-Gal:betaGlcNAc beta 1,3-galactosyltranferase-II [Mus musculus]	3e-08

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
226	AB014557	Homo sapiens mRNA for KIAA0657 protein, partial cds	1.5	1212992	(X90568) Protein sequence and annotation available soon via Swiss-Prot; available at present via e-mail from LABEIT@EMBL-Heidelberg.DE [Homo sapiens]	4e-13
227	AF000948	Borrelia burgdorferi oligopeptide permease homolog OppAIV (oppAIV) gene, complete cds	1.3	<NONE>	<NONE>	<NONE>
228	AF057287	Mus musculus RAB/Rip protein mRNA, partial cds	1.3	2498005	MYC PROTO-ONCOGENE PROTEIN (C-MYC) proto-oncogene [Sus scrofa]	2.6
229	U38951	Drosophila melanogaster vacuolar ATPase subunit E	1.1	<NONE>	<NONE>	<NONE>
230	AF027148	Homo sapiens myogenic determining factor 3	1.1	3172134	(U90209) RNA polymerase II largest subunit [Bonnemaisonia hamifera]	2.3
231	AF079310	Mus musculus histone deacetylase 3 (Hdac3) gene, exons 4 through 15 and complete cds	1.0	1657601	(U66220) unknown [Nannocystis exedens]	0.25
232	X52134	P.radiata lac gene for laccase	0.95	996020	(X91638) BRM protein [Gallus gallus]	0.31
233	D89016	Human mRNA for Neuroblastoma, complete cds	0.93	<NONE>	<NONE>	<NONE>
234	X76392	C.familiaris VIP36 (vesicular integral-membrane protein of 36 kDa) mRNA	0.93	4176446	(AL022238) dJ1042K10.2.1 (novel protein with probable rabGAP domains and Src homology domain 3)	7e-81
235	AF100694	Mus musculus Pontin52 mRNA, complete cds	0.90	<NONE>	<NONE>	<NONE>

SEQ ID	Nearest Neighbor (BlastN vs. Genbank) ACCESSION	DESCRIPTION	P VALUE	Nearest Neighbor (BlastX vs. Non-Redundant Proteins) ACCESSION	DESCRIPTION	P VALUE
236	AE000991	Archaeoglobus fulgidus section 116 of 172 of the complete genome	0.90	1176579	EGT2 PROTEIN PRECURSOR (EARLY G1 TRANSCRIPT 2) >gi|1362345|pir||S55862 probable membrane protein YNL327w - yeast (Saccharomyces cerevisiae) cerevisiae] >gi|1302445|gnl|PID|e239572 (Z71603) ORF YNL327w [Saccharomyces cerevisiae]	6.9
237	Z35922	S.cerevisiae chromosome II reading frame ORF YBR053c	0.86	<NONE>	<NONE>	<NONE>
238	U47331	Rattus norvegicus metabotropic glutamate receptor 4b mRNA, complete cds.	0.82	1550703	(Z80225) hypothetical protein Rv2662	4.1
239	X72810	H.sapiens Ig germline kappa-chain gene variable region (L3)	0.69	3023063	(AF052587) F14 [Xylella fastidiosa]	6.7
240	Z11700	Escherichia coli genes faeG, faeH, faeI, faeJ and IS629-like insertion sequence. > :: emb|Z11710|ECFAEHIJ E.coli faeH, faeI and faeJ genes encoding FaeH, FaeI and FaeJ proteins	0.69	2347188	(AC002338) laccase isolog [Arabidopsis thaliana] thaliana]	3.9
241	U71597	Phrynosoma douglassii NADH dehydrogenase subunit 4 (ND4) gene, mitochondrial gene encoding mitochondrial protein, partial cds	0.65	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
242	Z77798	Ammonia species LSU rRNA gene (partial; isolate Tr S 5; clone 16)	0.64	1174506	GLUTAMYL-TRNA SYNTHETASE glutamate--tRNA ligase (EC 6.1.1.17) - Haemophilus influenzae (strain Rd KW20) >gi|1573240 (U32713) glutamyl-tRNA synthetase (gltX) [Haemophilus influenzae Rd]	1.2
243	D25542	Human mRNA for golgi antigen gcp372, complete cds	0.64	111230	ultra-high-sulfur keratin 1 - mouse	1e-05
244	M80234	Cow dopamine transporter mRNA, putative cds.	0.64	3874972	(Z99709) similar to Elongation factor Tu family (contains ATP/GTP binding P-loop); cDNA EST EMBL:D76223 comes from this gene; cDNA EST yk478c5.5 comes from this gene [Caenorhabditis elegans]	8e-06
245	AB007918	Homo sapiens mRNA for KIAA0449 protein, partial cds	0.64	2833239	EPIDERMAL GROWTH FACTOR RECEPTOR KINASE SUBSTRATE EPS8 >gi|530823 (U12535) epidermal growth factor receptor kinase substrate [Homo sapiens]	2e-14
246	X51754	Human U266 rearranged DNA for lambda-immunoglobulin light chain	0.63	2072301	(U95102) mitotic phosphoprotein 90 [Xenopus laevis]	1.5
247	AE001554	Helicobacter pylori, strain J99 section 115 of 132 of the complete genome	0.62	<NONE>	<NONE>	<NONE>
248	Z64067	H.sapiens CpG DNA, clone 96e7, reverse read cpg96e7.rt1a .	0.62	<NONE>	<NONE>	<NONE>
249	AJ223768	Pinus sylvestris microsatellite DNA, clone SPAC11.5	0.62	<NONE>	<NONE>	<NONE>

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
250	AJ011592	Bacteriophage P1 ban gene	0.62	2493689	PHOTOSYSTEM II 10 KD PHOSPHOPROTEIN deltoides] >gi|2143326|gnl|PID|e319090 (Y13328) 10kDa phosphoprotein [Populus deltoides]	7.9
251	AF027151	Xenopus laevis survival of motor neuron protein interacting protein 1 (SIP1) mRNA, complete cds	0.62	4007790	(AL034463) putative single-strand polynucleotide binding protein [Schizosaccharomyces pombe]	2.0
252	AJ000376	Helobdella triserialis mRNA for actin	0.62	1117968	(U40763) CARS-Cyp [Homo sapiens] sapiens]	0.90
253	M69231	Rat thymosin beta 4 gene (pTB4G).intron.	0.62	4176370	(AC005058) similar to calcium-independent phospholipase A2; similar to AC004392 (PID:g3367519) [Homo sapiens]	6e-51
254	AB021638	Homo sapiens X11L2 mRNA for X11-like protein 2, complete cds	0.61	<NONE>	<NONE>	<NONE>
255	D26470	Bacteroides gingivalis DNA for arginyl endopeptidase, complete cds	0.61	<NONE>	<NONE>	<NONE>
256	J04737	A.thaliana ATPase gene, complete cds.	0.61	<NONE>	<NONE>	<NONE>
257	U06756	Bos taurus clone bm1308 microsatellite and are-1p repeat region.	0.61	1922280	(Y09905) snail like protein [Gallus gallus]	0.51
258	S75756	p15=cyclin D-dependent kinases 4 and 6-binding protein/p15 product {exon/intron 1} [human, brain tumors, Genomic, 753 nt]	0.61	484938	hypothetical protein 253 - Streptomyces griseus plasmid pSG1 (fragment)	0.13
259	L39837	Drosophila melanogaster tumor supressor (warts) mRNA exons 1-8, complete cds.	0.61	3875131	(Z70750) similar to vanadate resistance protein transmembranous domains [Caenorhabditis elegans]	1e-09

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
260	U52428	Human fatty acid synthase gene, partial cds	0.61	4226073	(AF125443) contains similarity to S. pombe phosphatidyl synthase (GB:Z28295) [Caenorhabditis elegans]	2e-26
261	X15292	Plasmodium falciparum gene for heat-shock protein pPf203	0.60	<NONE>	<NONE>	<NONE>
262	AB020663	Homo sapiens mRNA for KIAA0856 protein. partial cds	0.60	470341	(U00043) No definition line found [Caenorhabditis elegans]	5.7
263	U68723	Human checkpoint suppressor 1 mRNA, complete cds	0.60	544375	GALACTOSE-BINDING PROTEIN REGULATOR glucose/galactose binding protein regulator - Agrobacterium tumefaciens >gi|142228 (L10424) glucose/galactose binding protein regulator	5.7
264	M32687	S.griseus sporulation protein genes 1590 and 1422.	0.60	2582017	(AF012871) Merg1a' [Mus musculus]	3.3
265	AJ005331	Homo sapiens NKCC2 gene, exon 4, isoform B	0.60	3128353	(AF010496) maltose transport inner membrane protein	1.5
266	U14103	Mus musculus RGL protein mRNA, complete cds.	0.60	4099845	(U90533) serine protease inhibitor [Streptomyces fradiae]	0.098
267	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	0.59	3282851	(AF047897) ankyrin-like protein HGE-ANK [Ehrlichia sp. BDS]	5.5
268	AE000872	Methanobacterium thermoautotrophicum from bases 896604 to 912784 (section 78 of 148) of the complete genome	0.59	401553	HYPOTHETICAL 24.5 KD PROTEIN IN NADB-SRMB INTERGENIC REGION	4.3

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
269	L11871	Gallus gallus achaete-scute homologue (ASH) mRNA, complete cds.	0.59	628110	hypothetical protein - human herpesvirus 4 reading frame 1 [Human herpesvirus 4] 2 [Human herpesvirus 4] >gi|1334838|gnl|PID|e25079 4 [Human herpesvirus 4] >gi|1334840|gnl|PID|e25081 6 [Human herpesvirus 4] >gi|1334842|gnl|PID|e25067 8 [Human herpesvirus 4] >gi|1334844|gnl|PID|e25069 10 [Human herpesvirus 4] >gi|1334846|gnl|PID|e25071 12 [Human herpesvirus 4]	4.2
270	AF017114	Oryctolagus cuniculus glycogen synthase mRNA, complete cds	0.59	728856	NITROGENASE IRON-IRON PROTEIN ALPHA CHAIN (NITROGENASE COMPONENT I) (DINITROGENASE) capsulatus >gi|312238 (X70033) alternative nitrogenase	2.4
271	AF027807	Homo sapiens beta-casein (CSN2) gene, complete cds	0.59	3252932	(AF067155) truncated rev protein [Human immunodeficiency virus type 1]	1.5
272	U81787	Human Wnt10B mRNA, complete cds	0.59	3875538	(Z67990) similar to cuticle collagen	1.4
273	U76036	Apteryx australis 16S ribosomal RNA gene, mitochondrial gene for mitochondrial RNA, partial sequence	0.59	4193356	(AF055088) ATP-binding cassette; PsaB [Streptococcus pneumoniae]	0.83
274	AB014564	Homo sapiens mRNA for KIAA0664 protein, partial cds	0.59	1709851	PTB-ASSOCIATED SPLICING FACTOR (PSF) long form - human >gi|38458 (X70944) PTB-associated splicing factor [Homo sapiens]	0.17
275	AF044171	Homo sapiens cyclin-dependent kinase inhibitor 2D (CDKN2D) gene, partial cds	0.59	3925213	(AL032626) Y37D8A.17 [Caenorhabditis elegans]	3e-10

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
276	L19640	Saccharomyces cerevisiae cdc2/cdc28 related protein kinase gene, complete cds.	0.59	3880115	(Z81130) T23G11.9 [Caenorhabditis elegans]	1e-21
277	Z80999	Human DNA sequence from cosmid E140G5 on chromosome 22, complete sequence [Homo sapiens]	0.58	<NONE>	<NONE>	<NONE>
278	Y11108	H.sapiens WNT8B gene	0.58	<NONE>	<NONE>	<NONE>
279	U80001	Sphyraena idiastes lactate dehydrogenase A	0.58	<NONE>	<NONE>	<NONE>
280	Z49637	S.cerevisiae chromosome X reading frame ORF YJR137c	0.58	<NONE>	<NONE>	<NONE>
281	X64467	H.sapiens ALAD gene for porphobilinogen synthase	0.58	<NONE>	<NONE>	<NONE>
282	X74506	G.gallus hox B3 mRNA	0.58	<NONE>	<NONE>	<NONE>
283	U68040	Cochliobolus heterostrophus polyketide synthase	0.58	<NONE>	<NONE>	<NONE>
284	AF089084	Arabidopsis thaliana putative auxin efflux carrier protein (PIN1) mRNA, complete cds	0.58	<NONE>	<NONE>	<NONE>
285	U38481	Rattus norvegicus ROK-alpha mRNA, complete cds	0.58	<NONE>	<NONE>	<NONE>
286	AF017656	Homo sapiens G protein beta 5 subunit mRNA, complete cds	0.58	3236249	(AC004684) hypothetical protein [Arabidopsis thaliana]	9.2
287	M96234	Human glutathione transferase class mu number 4 .	0.58	1280073	(U55366) Similar to cuticle collagen [Caenorhabditis elegans]	7.1
288	AB002339	Human mRNA for KIAA0341 gene, partial cds	0.58	861293	(U28741) F35D2.1 gene product [Caenorhabditis elegans]	7.1

SEQ ID	Nearest Neighbor (BlastN vs. Genbank) ACCESSION	DESCRIPTION	P VALUE	Nearest Neighbor (BlastX vs. Non-Redundant Proteins) ACCESSION	DESCRIPTION	P VALUE
289	U11295	Neisseria gonorrhoeae carbamoyl phosphate synthetase (glutamine) small subunit (carA) and large subunit (carB) genes, complete cds.	0.58	2425135	(AF020283) DG2044 gene product [Dictyostelium discoideum]	5.3
290	D80001	Human mRNA for KIAA0179 gene, partial cds	0.58	4097223	(U49836) gamma-glutamyl transpeptidase precursor [Brugia malayi]	4.1
291	Z11700	Escherichia coli genes faeG, faeH, faeI, faeJ and IS629-like insertion sequence. > :: emb|Z11710|ECFAEHIJ E.coli faeH, faeI and faeJ genes encoding FaeH, FaeI and FaeJ proteins	0.58	2347188	(AC002338) laccase isolog [Arabidopsis thaliana] thaliana]	3.2
292	M77350	Mouse hair keratin A1 (MHKA1) gene, complete cds.	0.58	141165	HYPOTHETICAL 8.3 KD PROTEIN >gi|62179	3.2
293	X63787	T.thermophila gene for snRNA U3-2	0.58	2826900	(AB004461) DNA polymerase alpha catalytic subunit [Oryza sativa]	3.1
294	D63881	Human mRNA for KIAA0160 gene, partial cds	0.58	1934730	(U95036) germin-like protein [Arabidopsis thaliana]	3.1
295	U39378	Gymnocarena mexicana 16S ribosomal RNA gene, mitochondrial gene encoding mitochondrial RNA, partial sequence	0.58	2194131	(AC002062) Similar to Synechocystis antiviral protein	3.1
296	X87987	P.pastoris PRC1 gene > :: dbj|E12103|E12103 DNA encoding precursor of protease from Pichia pastoris	0.58	3914197	OCCLUDIN >gi|1276983 (U49221) occludin [Canis familiaris] >gi|1589181|prf||2210347D occludin [Canis familiaris]	3.1

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
297	X75782	A.thaliana (L.Heynh.) chloroplast mRNA for recombinant APS-kinase	0.58	1732444	(D38529) DRPLA protein [Homo sapiens]	2.4
298	M64848	Mouse platelet-derived growth factor B chain musculus platelet-derived growth factor beta-chain (sis) gene, exon 5.	0.58	3025832	(AF055985) pyrrolidone-rich antigen [Onchocerca volvulus]	1.4
299	AE001460	Helicobacter pylori, strain J99 section 21 of 132 of the complete genome	0.58	2827198	(AF037454) ubiquitin protein ligase [Mus musculus]	1.1
300	X65720	M.musculus gene for protein kinase C-gamma (exon1 and exon 2)	0.58	418395	CHD1 PROTEIN >gi|320737|pir||S30818 hypothetical protein YER164w - yeast (Saccharomyces cerevisiae) >gi|603404 (U18917) Chd1p: transcriptional regulator [Saccharomyces cerevisiae]	1.1
301	AF043130	Arabidopsis thaliana lactate dehydrogenase	0.58	3024637	SEX-DETERMINING REGION Y PROTEIN determining protein [Mus	0.62
302	D28116	Human genes for collagen type IV alpha 5 and 6, exon 1 and exon 1'	0.58	1458250	(U64835) T09D3.3 [Caenorhabditis elegans]	0.36
303	AE001075	Archaeoglobus fulgidus section 32 of 172 of the complete genome	0.58	2276333	(Z97991) hypothetical protein Rv0336	0.36
304	AF003948	Rhodococcus opacus chloromuconate cycloisomerase transposase homolog genes, complete cds	0.58	477072	mucin 7 precursor, salivary - human	0.28
305	U10692	Human MAGE-7 antigen (MAGE7) pseudogene, complete cds.	0.58	3287858	HOMEOBOX PROTEIN HOX-C11	0.054

[illegible]	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
306	AF003948	Rhodococcus opacus chloromuconate cycloisomerase transposase homolog genes, complete cds	0.58	3551821	(AF058803) mucin 4 [Homo sapiens]	0.041
307	X99350	H.sapiens HFH4 gene, exon 1 and joined CDS	0.58	137483	VAV PROTO-ONCOGENE >gi|55221 (X64361) proto-oncogene [Mus musculus]	0.024
308	AJ234282	Homo sapiens mRNA for Ig heavy chain variable region, clone C	0.58	3264846	(AC003682) R27945_2 [Homo sapiens]	0.018
309	AF079310	Mus musculus histone deacetylase 3 (Hdac3) gene, exons 4 through 15 and complete cds	0.58	1657601	(U66220) unknown [Nannocystis exedens]	0.014
310	AF019367	Human thiopurine methyltransferase (TPMT) gene, exons 6 and 7	0.58	3283352	(AF063020) lens epithelium-derived growth factor [Homo sapiens]	0.011
311	X65720	M.musculus gene for protein kinase C-gamma (exon1 and exon 2)	0.58	1790878	(U38291) microtubule-associated protein 1a [Homo sapiens]	0.008
312	AB011155	Homo sapiens mRNA for KIAA0583 protein, partial cds	0.58	1351166	SYNAPSINS IA AND IB >gi|163713	0.006
313	X63692	H.sapiens mRNA for DNA	0.58	1817548	(D84307) phosphoethanolamine cytidylyltransferase [Homo sapiens]	0.001
314	U53746	Feline immunodeficiency virus isolate FIV-Pco336-8 pol polyprotein (pol) gene, partial cds	0.58	2246532	(U93872) ORF 73, contains large complex repeat CR 73	2e-05
315	K00436	Rattus norvegicus (clone rt1-1) pseudo-Gly-tRNA gene.	0.58	206712	(M64793) salivary proline-rich protein [Rattus norvegicus]	1e-05

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
316	S79632	HSF2=heat shock factor 2 {alternatively spliced, splice junction region} [mice, CBA/J, testis, Genomic, 120 nt, segment 2 of 3]	0.58	4038594	(AJ222798) tDET1 protein [Lycopersicon esculentum]	3e-06
317	D43964	Rat liver mRNA for Kan-1, complete cds	0.58	1280135	(U55376) coded for by C. elegans cDNA cm21e6; coded for by C. elegans cDNA cm01e2; similar to melibiose carrier protein (thiomethylgalactoside permease II)	1e-08
318	AB007918	Homo sapiens mRNA for KIAA0449 protein, partial cds	0.58	2833239	EPIDERMAL GROWTH FACTOR RECEPTOR KINASE SUBSTRATE EPS8 >gi|530823 (U12535) epidermal growth factor receptor kinase substrate [Homo sapiens]	3e-13
319	AB001466	Homo sapiens mRNA for Efs1, complete cds	0.58	2943716	(D45027) 25 kDa trypsin inhibitor [Homo sapiens]	2e-14
320	Z11701	Saccharomyces cerevisiae IRE1 gene for putative protein kinase.	0.58	3880115	(Z81130) T23G11.9 [Caenorhabditis elegans]	9e-21
321	Z49535	S.cerevisiae chromosome X reading frame ORF YJR035w	0.58	4106562	(Z83819) dJ146H21.2 (similar to CYTOCHROME B-245 HEAVY CHAIN) [Homo sapiens]	3e-33
322	M62506	S.cerevisiae DBF20 gene, complete cds.	0.57	<NONE>	<NONE>	<NONE>
323	X05944	Yeast PSS gene for phosphatidylserine synthetase	0.57	<NONE>	<NONE>	<NONE>
324	D38536	Snail gene for ADP-ribosyl cyclase, complete cds	0.57	<NONE>	<NONE>	<NONE>
325	Z75004	S.cerevisiae chromosome XV reading frame ORF YOR096w	0.57	<NONE>	<NONE>	<NONE>
326	L77034	Homo sapiens (subclone 10_e10 from P1 H16) DNA sequence.	0.57	<NONE>	<NONE>	<NONE>

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
327	D37887	Cyprinus carpio c-myc gene for c-Myc, complete cds	0.57	<NONE>	<NONE>	<NONE>
328	AB014562	Homo sapiens mRNA for KIAA0662 protein, partial cds	0.57	197406	(M57576) Ig kappa chain [Mus musculus]	8.9
329	Z69651	Human DNA sequence from cosmid L75B9, Huntington's Disease Region, chromosome 4p16.3	0.57	1079280	chaperonin containing TCP-1 complex gamma chain - African clawed frog >gi|793886 (X84990) Cctg	8.9
330	D89285	Mesocricetus auratus mRNA for inter-alpha trypsin inhibitor heavy chain 1, complete cds	0.57	134132	RYANODINE RECEPTOR, SKELETAL MUSCLE	6.9
331	Z48951	S.cerevisiae chromosome XVI cosmid 9723	0.57	4210432	(AJ130783) APC2 protein [Mus musculus]	5.3
332	X95573	A.thaliana mRNA for salt-tolerance zinc finger protein	0.57	1174828	TYROSINE DECARBOXYLASE 2 4.1.1.25) - parsley >gi|169671 (M96070) tyrosine decarboxylase [Petroselinum	5.2
333	U95094	Xenopus laevis XL-INCENP (XL-INCENP) mRNA, complete cds	0.57	465646	PROBABLE ABC TRANSPORTER ATP-BINDING PROTEIN IN NTRA/RPON 5'REGION (ORF1) Azorhizobium caulinodans >gi|311388 (X69959) ORF1	4.0
334	AE001116	Borrelia burgdorferi (section 2 of 70) of the complete genome	0.57	2314735	(AE000653) Na+/H+ antiporter (nhaA) [Helicobacter pylori 26695]	4.0
335	Z34291	R.norvegicus mRNA for putative chloride channel.	0.57	1350832	DNA-DIRECTED RNA POLYMERASE I SECOND LARGEST SUBUNIT (RNA POLYMERASE I SUBUNIT 2) chain RPA2 - Euplotes octocarinatus (SGC9) >gi|578407 octocarinatus]	3.0

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
336	D88255	Homo sapiens A30 Vk germline gene, partial cds	0.57	3875983	(Z81063) similar to Actinin-type actin-binding domain containing proteins [Caenorhabditis elegans]	3.0
337	AF037261	Homo sapiens SH3-containing adaptor molecule-1 mRNA, complete cds	0.57	1397341	(U61955) similar to kinesin-like protein; coded for by C. elegans cDNA yk184h5.3; coded for by C. elegans cDNA yk184h5.5; coded for by C. elegans cDNA yk13d7.3; coded for by C. elegans cDNA yk13d7.5; coded for by C. elegans cDNA yk31e1.5; co... >gi|3493541 (AF057567) kinesin-like protein ZEN-4a [Caenorhabditis elegans]	2.3
338	U26595	Rattus norvegicus prostaglandin F2a receptor regulatory protein precursor, mRNA, complete cds	0.57	2773160	(AF039656) neuronal tissue-enriched acidic protein [Homo sapiens]	2.3
339	X69903	R.norvegicus mRNA for interleukin 4 receptor	0.57	2649193	(AE001009) quinone-reactive Ni/Fe-hydrogenase B-type cytochrome subunit (hydC) [Archaeoglobus fulgidus]	1.8
340	Z74825	S.cerevisiae chromosome XV reading frame ORF YOL083w	0.57	1458319	(U64846) F47D2.5 gene product [Caenorhabditis elegans]	1.4
341	AJ131469	Foot-and-mouth disease virus O vp1 gene, strain O/A/58	0.57	91206	proline-rich protein - mouse (fragment) musculus]	1.4
342	AF011360	Mus musculus regulator of G-protein signaling 7 (RGS7) mRNA, complete cds	0.57	542514	gelsolin - American lobster	0.80
343	AF011360	Mus musculus regulator of G-protein signaling 7 (RGS7) mRNA, complete cds	0.57	1078946	gelsolin - American lobster >gi|452313 gelsolin [Homarus americanus]	0.80

SEQ ID	Nearest Neighbor (BlastN vs. Genbank) ACCESSION	DESCRIPTION	P VALUE	Nearest Neighbor (BlastX vs. Non-Redundant Proteins) ACCESSION	DESCRIPTION	P VALUE
344	L39210	Homo sapiens inosine monophosphate dehydrogenase type II gene, complete cds	0.57	559526	(X77466) 98.8kD polyprotein [Strawberry latent ringspot virus]	0.79
345	U81523	Human endometrial bleeding associated factor mRNA, complete cds	0.57	211499	(K01702) HMW/LMW collagen subunit precursor [Gallus gallus]	0.79
346	U46561	Tetrahymena thermophila polyubiquitin (TTU3) gene, complete cds, and RNA polymerase II subunit 2 (RPB2) gene, partial cds	0.57	2506493	HYPOTHETICAL 100.5 KD PROTEIN IN IAP-CYSH INTERGENIC REGION >gi|882654 (U29579) alternate gene name ygcB; ORF_f888 [Escherichia coli] >gi|1789119	0.60
347	X95543	C.japonica mRNA for legumin (clone CjLeg31)	0.57	1709261	NEUROFILAMENT TRIPLET M PROTEIN (160 KD NEUROFILAMENT PROTEIN) (NF-M) >gi|1083164|pir||S55395 neurofilament protein M - rabbit (fragment) >gi|854353	0.46
348	Y17282	Homo sapiens mRNA for cytokeratin type II	0.57	3044086	(AF055904) unknown [Myxococcus xanthus]	0.45
349	X00716	Frog mRNA fragment for alpha-A2-crystallin	0.57	3406654	(AF079369) transcriptional repressor TUP1 [Dictyostelium discoideum]	0.20
350	X53238	Klebsiella sp. bacteriophage K11 gene 1 for RNA polymerase	0.57	1228093	(Z46913) polyketide synthase	0.16
351	X99012	H.sapiens FUS gene, exon 12	0.57	243898	(S78897) GOR=antigenic epitope [chimpanzees, Peptide, 427 aa] [Pan]	0.090
352	AL008711	Human DNA sequence from PAC 390N22 on chromosome Xp22.2	0.57	1469545	(U53585) fibronectin attachment protein [Mycobacterium avium]	0.053
353	S74506	SOX9 [human, fetal brain, Genomic, 1494 nt, segment 3 of 3]	0.57	1326350	(U58748) similar to potential transmembrane domains in S. cerevisiae nulcear division RFT1 protein (SP:P38206)	0.017

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
354	D25542	Human mRNA for golgi antigen gcp372, complete cds	0.57	4063399	(AF102575) cell surface protein DTFA [Dictyostelium discoideum]	0.005
355	AB015426	Mus musculus mRNA for alpha1,3-fucosyltransferase IX, complete cds	0.57	2661842	(Y15732) DNA polymerase beta [Xenopus laevis]	7e-11
356	X51394	Xenopus mRNA for APEG protein, containing a highly repetitive amino acid sequence	0.57	1929056	(Y12090) putative 3,4-dihydroxy-2-butanone kinase [Lycopersicon esculentum]	9e-12
357	AB007918	Homo sapiens mRNA for KIAA0449 protein, partial cds	0.57	2833239	EPIDERMAL GROWTH FACTOR RECEPTOR KINASE SUBSTRATE EPS8 >gi|530823 (U12535) epidermal growth factor receptor kinase substrate [Homo sapiens]	3e-13
358	AB001466	Homo sapiens mRNA for Efs1, complete cds	0.57	2943716	(D45027) 25 kDa trypsin inhibitor [Homo sapiens]	2e-14
359	Y00760	Rabbit mRNA for adult fast skeletal troponin-C	0.57	2576348	(AC002400) Glutamyl tRNA synthetase [Homo sapiens]	2e-28
360	X95153	H.sapiens brca2 gene exon 3 > :: emb|A62778|A62778 Sequence 19 from Patent WO9719110	0.57	3419847	(AC004982) similar to yeast hypothetical protein ybk4; similar to P38164 (PID:g586461) [Homo sapiens]	2e-55
361	X85967	B.vulgaris mRNA for betavulgin	0.56	<NONE>	<NONE>	<NONE>
362	U09251	Mycoplasma genitalium DNA gyrase subunit B complete cds, DNA polymerase III beta subunit (dnaN) and seryl-tRNA synthetase (serS) genes, partial cds.	0.56	<NONE>	<NONE>	<NONE>
363	V00158	Chloroplast Euglena gracilis genes coding for transfer RNAs specific for threonine, glycine, methionine, serine and glutamine.	0.56	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
364	D88151	Clostridium perfringens DNA for D-alanine:D-alanine ligase, cortical fragment-lytic enzyme	0.56	<NONE>	<NONE>	<NONE>
365	U67478	Methanococcus jannaschii section 20 of 150 of the complete genome	0.56	<NONE>	<NONE>	<NONE>
366	L23800	Tachyglossus aculeatus beta-globin homolog (HBB) gene, complete cds	0.56	<NONE>	<NONE>	<NONE>
367	AB011129	Homo sapiens mRNA for KIAA0557 protein, partial cds	0.56	<NONE>	<NONE>	<NONE>
368	L77034	Homo sapiens (subclone 10_e10 from P1 H16) DNA sequence.	0.56	<NONE>	<NONE>	<NONE>
369	Z47202	C.albicans gene for TFIIIB (BRF1) subunit.	0.56	<NONE>	<NONE>	<NONE>
370	U53868	Clostridium acetobutylicum mannitol-specific phosphotransferase system (PTS) system, mtlA, mtlR, mtlF, and mtlD genes, complete cds	0.56	<NONE>	<NONE>	<NONE>
371	AF041259	Homo sapiens breast cancer putative transcription factor (ZABC1) mRNA, complete cds	0.56	<NONE>	<NONE>	<NONE>
372	L42636	Plasmodium falciparum variant-specific surface protein (var-7) mRNA, complete cds.	0.56	2213557	(Z97052) hypothetical protein	8.8

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
373	U96180	Human protein tyrosine phosphatase (TEP1) mRNA, complete cds	0.56	731016	THIOREDOXIN REDUCTASE thioredoxin reductase (NADPH) [Coxiella burnetii]	8.7
374	L76259	Homo sapiens PTS gene, complete cds	0.56	2369863	(Y12225) Spi-1/PU.1 transcription factor	6.7
375	AF045946	Mus musculus D16Jhu17 YAC 98B3 acentric end, partial sequence	0.56	2130017	hypothetical protein - common sunflower protein [Helianthus annuus]	5.1
376	X97986	M.musculus mRNA for desmocollin type 1	0.56	4038031	(AC005936) hypothetical protein [Arabidopsis thaliana]	3.9
377	X79437	M.musculus whey acidic protein (WAP) gene, exon 1	0.56	549670	SPINDLE POLE BODY COMPONENT SPC42 yeast (Saccharomyces cerevisiae) >gi|486054 (Z28042) ORF YKL042w [Saccharomyces cerevisiae] >gi|666098 (X71621) hypothetical 42.3 kD protein [Saccharomyces cerevisiae]	3.9
378	M27902	Rat cardiac specific sodium channel alpha-subunit mRNA, complete cds.	0.56	585234	ENDOGLUCANASE G PRECURSOR 3.2.1.-) CelCCG precursor - Clostridium cellulolyticum cellulolyticum]	3.9
379	AF036696	Caenorhabditis elegans cosmid F15B10	0.56	546071	gp70=envelope protein {endogenous provirus} host=cat lymphoid tissues, Peptide, 445 aa]	3.6
380	Z99102	Caenorhabditis elegans cosmid B0331, complete sequence [Caenorhabditis elegans]	0.56	603664	(U14101) putative reverse transcriptase; ORF2; encodes aa motifs conserved in reverse transcriptases; most closely related reverse transcriptases are those of non-LTR retrotransposons. The 3' 901 bp of this CDS are identical to the 3' 901 bp ...	3.0
381	L27850	Equus caballus (clone T131) T-cell receptor DNA, V-region.	0.56	1079150	transcription factor shn - fruit fly	1.7

SEQ ID	Nearest Neighbor (BlastN vs. Genbank) ACCESSION	DESCRIPTION	P VALUE	Nearest Neighbor (BlastX vs. Non-Redundant Proteins) ACCESSION	DESCRIPTION	P VALUE
382	X97986	M.musculus mRNA for desmocollin type 1	0.56	2497227	HYPOTHETICAL 113.1 KD PROTEIN IN PRE5-FET4 INTERGENIC REGION >gi|1072409 (Z54141) unknown	1.7
383	AF087455	Didelphis virginiana G protein receptor kinase 2 mRNA, complete cds	0.56	1213453	(U12964) contains ankyrin-like repeats; similar to human desmoplakin repeat region [Caenorhabditis elegans]	1.3
384	D80011	Human mRNA for KIAA0189 gene, complete cds	0.56	226535	protease [Hepatitis B virus]	1.1
385	AJ002272	Mus musculus mRNA for HAP1-A protein, 3' region	0.56	3327158	(AB014572) KIAA0672 protein [Homo sapiens]	1.0
386	L39210	Homo sapiens inosine monophosphate dehydrogenase type II gene, complete cds	0.56	628431	coat protein - strawberry latent ringspot virus	0.77
387	X02770	Mouse Thy-1.2 gene 5' untranslated region and exon 1	0.56	3327046	(AB014516) KIAA0616 protein [Homo sapiens]	0.59
388	AF038575	Schizosaccharomyces pombe Wiskott-Aldrich Syndrome protein homolog (wsp1+) gene, complete cds, and BTF3/beta-NAC gene, partial sequence	0.56	88466	salivary proline-rich phosphoprotein precursor PRH1 (allele PIF) - human >gi|190484 (K03203) prepro salivary proline-rich protein [Homo sapiens] >gi|190512	0.35
389	X56747	Rat mRNA for fetal intestinal lactase-phlorizin hydrolase precursor, partial	0.56	2072742	(Z48674) chitinase homologue [Sesbania rostrata]	0.23
390	Y12072	G.arboreum mRNA for farnesyl pyrophosphate synthase	0.56	296670	(X07882) Po protein [Homo sapiens]	0.20
391	S75756	p15=cyclin D-dependent kinases 4 and 6-binding protein/p15 product {exon/intron 1} [human, brain tumors, Genomic, 753 nt]	0.56	1082743	protein kinase (EC 2.7.1.37) SPRK - human sapiens] >gi|1090771|prf||2019437A protein Tyr kinase I	0.15

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
392	U62528	Equus caballus type II collagen mRNA, complete cds	0.56	461671	[Segment 1 of 2] COLLAGEN ALPHA 1(I) CHAIN	0.030
393	X96877	C.reinhardtii mRNA for unknown lumenal polypeptide	0.56	3341678	(AC003672) putative zinc finger protein [Arabidopsis thaliana]	5e-09
394	S78788	cGATA-3 [chickens, liver, Genomic, 979 nt, segment 4 of 4]	0.56	2661590	(AL009196) 1-evidence=predicted by content; 1-method=genefinder;084; 1-method_score=59.41; 1-evidence_end; 2-evidence=predicted by match; 2-match_accession=AA950019; 2-match_description=LD29959.5prime LD Drosophila melanogas...	2e-11
395	AF006640	Drosophila melanogaster Ste20-like protein kinase mRNA, complete cds	0.56	1109830	(U41534) coded for by C. elegans cDNA CEESI42F; Similar to helicases of SNF2/RAD54 family. [Caenorhabditis elegans]	6e-12
396	AF006640	Drosophila melanogaster Ste20-like protein kinase mRNA, complete cds	0.56	1109830	(U41534) coded for by C. elegans cDNA CEESI42F; Similar to helicases of SNF2/RAD54 family. [Caenorhabditis elegans]	4e-13
397	AE000716	Aquifex aeolicus section 48 of 109 of the complete genome	0.56	3688350	(AL030996) dJ1189B24.4 (novel PUTATIVE protein similar to hypothetical proteins S. pombe C22F3.14C and C. elegans C16A3.8) [Homo sapiens]	3e-66
398	Z36079	S.cerevisiae chromosome II reading frame ORF YBR210w	0.55	<NONE>	<NONE>	<NONE>
399	Y17267	Mus musculus mRNA for ubiquitin conjugating enzyme	0.55	<NONE>	<NONE>	<NONE>
400	AC001461	Homo sapiens (subclone 2_g5 from BAC H107) DNA sequence	0.55	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
401	AF019079	Alouatta seniculus breast and ovarian susceptibility (BRCA1) gene, partial cds	0.55	<NONE>	<NONE>	<NONE>
402	M90058	Human serglycin gene, exons 1,2, and 3.	0.55	<NONE>	<NONE>	<NONE>
403	AB013469	Mus musculus CLM2 gene for cytohesin 2, complete and partial cds, alternative splicing	0.55	1729760	(Z68152) chitinase [Gossypium hirsutum]	8.6
404	AJ011592	Bacteriophage P1 ban gene	0.55	2493689	PHOTOSYSTEM II 10 KD PHOSPHOPROTEIN deltoides] >gi|2143326|gnl|PID|e319090 (Y13328) 10kDa phosphoprotein [Populus deltoides]	6.6
405	Z15118	T.brucei kinetoplast maxicircle variable region DNA	0.55	2970432	(AF049132) NADH dehydrogenase subunit 5 [Florometra serratissima]	6.5
406	Z48951	S.cerevisiae chromosome XVI cosmid 9723	0.55	4210432	(AJ130783) APC2 protein [Mus musculus]	4.9
407	U78726	Homo sapiens mad protein homolog Smad2 gene, promoter, exon 1a and exon 1b	0.55	3319290	(AF055994) thyroid hormone receptor-associated protein complex component TRAP220 [Homo sapiens]	4.9
408	AG001389	Homo sapiens genomic DNA, 21q region, clone: 9H11Bm42	0.55	125684	KRUEPPEL PROTEIN >gi|72899|pir||TWFF Krueppel gap protein - fruit fly (Drosophila sp.) melanogaster] >gi|224875|prf||1202348A Krueppel gene	3.8
409	M27640	Plasmodium vivax major blood stage surface antigen gene, partial cds.	0.55	549453	X-LINKED PEST-CONTAINING TRANSPORTER transporter - human >gi|458255 (U05321) X-linked PEST-containing transporter [Homo sapiens]	3.8

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
410	D37977	Fugu rubripes mRNA for sodium channel alpha subunit, partial cds	0.55	1435038	(D38024) ORF [Homo sapiens]	3.7
411	M88505	Ostertagia ostertagi cathepsin B-like cysteine protease gene, partial cds.	0.55	3941277	(AF000900) p45 [Rattus norvegicus]	2.9
412	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.55	2570154	(AB008376) 17-kDa PKC-potentiated inhibitory protein of PP1 [Sus scrofa]	2.8
413	U89241	Human mibp gene, partial cds	0.55	4097465	(U62253) 16kDa secretory protein [Sus scrofa]	2.2
414	AF027151	Xenopus laevis survival of motor neuron protein interacting protein 1 (SIP1) mRNA, complete cds	0.55	4007790	(AL034463) putative single-strand polynucleotide binding protein [Schizosaccharomyces pombe]	1.7
415	AF006821	Bufo marinus natriuretic peptide receptor C mRNA, partial cds	0.55	2245075	(Z97343) GTP-binding RAB2A protein	1.7
416	Y12736	Lactococcus lactis cremoris plasmid pJW565 DNA, llabiiM, llabiiR genes and orfX	0.55	3386334	(AF035120) type I procollagen pro-alpha 2 chain [Canis familiaris]	1.3
417	U38307	Mus musculus collagen alpha-1 type 1 gene, 5' flanking region, partial sequence.	0.55	1362802	gastric mucin - human (fragment) >gi|547517	1.3
418	D13473	Mouse mRNA for Rad51 protein	0.55	1374698	(D83032) nuclear protein, NP220 [Homo sapiens]	1.3
419	AF045238	Bungarus fasciatus acetylcholinesterase gene, alternatively spliced products, partial cds	0.55	3261734	(Z94752) hypothetical protein Rv1004c	0.99
420	AE000795	Methanobacterium thermoautotrophicum from bases 1 to 10208 (section 1 of 148) of the complete genome	0.55	186396	(M94131) mucin [Homo sapiens]	0.97

SEQ ID	Nearest Neighbor (BlastN vs. Genbank) ACCESSION	DESCRIPTION	P VALUE	Nearest Neighbor (BlastX vs. Non-Redundant Proteins) ACCESSION	DESCRIPTION	P VALUE
421	X99537	Y.lipolytica SEC62 gene	0.55	3876397	(Z81068) F25H5.2 [Caenorhabditis elegans]	0.58
422	U08147	Aquilegia sp. phytochrome (PHYB/D) gene, partial cds.	0.55	2338024	(AF005370) ribonucleotide-reductase, large subunit	0.57
423	Z56586	H.sapiens CpG DNA, clone 12c8, reverse read cpg12c8.rt1d .	0.55	3320122	(U46007) espin [Rattus norvegicus]	0.44
424	U39442	Mus musculus glutamine:fructose-6-phosphate amidotransferase (GFAT) gene, 5' region and partial cds	0.55	282600	hypothetical protein - Mycoplasma hyorhinis	0.43
425	K02298	Rat chymotrypsin B (chyB) gene, complete cds.	0.55	3413810	(Y17034) Bassoon [Mus musculus]	0.33
426	X84792	M.musculus clusterin gene	0.55	1652475	(D90905) hypothetical protein	0.25
427	U00185	Capra aegagrus Saanen and Weisse Edel breeds DR beta-chain antigen binding domain, MHC class II DRB	0.55	2507136	SUBTILIN BIOSYNTHESIS PROTEIN SPAB	0.19
428	Z54946	H.sapiens CpG DNA, clone 178a12, reverse read cpg178a12.rt1a .	0.55	807646	(M17294) unknown protein [Human herpesvirus 4]	0.065
429	AF031650	Oryctolagus cuniculus anion exchanger 3 brain isoform (AE3) mRNA, complete cds	0.55	1778210	(U68412) fibrillar collagen [Arenicola marina]	0.044
430	M25579	Bovine adenylyl cyclase Type I mRNA, complete cds.	0.55	2649040	(AE000997) conserved hypothetical protein [Archaeoglobus fulgidus]	0.023
431	Z48796	H.sapiens Ski-W mRNA for helicase	0.55	330452	(M14708) DNA polymerase [Human cytomegalovirus]	0.023

SEQ ID	Nearest Neighbor (BlastN vs. Genbank) ACCESSION	DESCRIPTION	P VALUE	Nearest Neighbor (BlastX vs. Non-Redundant Proteins) ACCESSION	DESCRIPTION	P VALUE
432	M80234	Cow dopamine transporter mRNA, putative cds.	0.55	3874972	(Z99709) similar to Elongation factor Tu family (contains ATP/GTP binding P-loop); cDNA EST EMBL:D76223 comes from this gene; cDNA EST yk478c5.5 comes from this gene [Caenorhabditis elegans]	4e-04
433	U91616	Human I kappa B epsilon (IkBe) mRNA, complete cds	0.55	3875577	(Z68314) similar to G-protein; cDNA EST EMBL:C11959 comes from this gene; cDNA EST EMBL:C10341 comes from this gene; cDNA EST yk494e4.3 comes from this gene; cDNA EST yk448a8.5 comes from this gene comes from this gene; cDNA EST EMBL:C10341 comes from this gene; cDNA EST yk494e4.3 comes from this gene; cDNA EST yk448a8.5 comes from this gene [Caenorhabditis elegans] >gi|3880364|gnl|PID|e1349948 (Z83016) similar to G-protein; cDNA EST EMBL:C11959 comes from this gene; cDNA EST EMBL:C10341 comes from this gene; cDNA EST yk494e4.3 comes from this gene; cDNA EST yk448a8.5 comes from this gene [Caenorhabditis elegans]	7e-06
434	D10910	Arabidopsis thaliana Atpk7 gene for serine/threonine protein kinase, complete cds	0.55	3876072	(Z81505) Similarity to Metanococcus hypothetical protein 0682 (TR:Q58095) [Caenorhabditis elegans]	4e-42
435	L22013	Swinepox virus complete ORFS C20L-C1L > :: gb|I58297|I58297 Sequence 14 from patent US 5651972	0.54	<NONE>	<NONE>	<NONE>
436	Z92653	Human immunodeficiency virus type 1 env gene	0.54	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
437	K01992	E.coli phosphate-repressible periplasmic phosphate-binding protein (phoS), peripheral membrane proteins (pstC, pstB and phoU) and integral membrane protein (pstA) genes, complete cds.	0.54	<NONE>	<NONE>	<NONE>
438	AE001415	Plasmodium falciparum chromosome 2, section 52 of 73 of the complete sequence	0.54	<NONE>	<NONE>	<NONE>
439	AF064030	Helianthus tuberosus lectin 2 mRNA, complete cds	0.54	<NONE>	<NONE>	<NONE>
440	X12591	E.coli plasmid DNA for colicin E9	0.54	<NONE>	<NONE>	<NONE>
441	U73679	Caenorhabditis elegans YNK1-a mRNA, complete cds	0.54	<NONE>	<NONE>	<NONE>
442	Z93990	Unidentified bacterium DNA for 16S ribosomal RNA	0.54	<NONE>	<NONE>	<NONE>
443	X85967	B.vulgaris mRNA for betavulgin	0.54	757836	(Z37980) ORF12 [Escherichia coli]	8.3
444	U76524	Sambucus nigra ribosome inactivating protein precursor mRNA, complete cds	0.54	151377	(M80653) tetraheme [Pseudomonas stutzeri]	6.2
445	X71800	H.sapiens gene for 5S rRNA (640 bp) > :: emb|X71801|HS5SR640B H.sapiens gene for 5S rRNA (640 bp)	0.54	3322653	(AE001216) T. pallidum predicted coding region TP0369	2.7
446	U89241	Human mibp gene, partial cds	0.54	4097465	(U62253) 16kDa secretory protein [Sus scrofa]	2.2

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
447	L16013	Rattus norvegicus Q-like gene sequence	0.54	3087760	(AJ005583) p75 protein [Crypthecodinium cohnii]	0.95
448	U60275	Capra hircus skeletal muscle voltage-gated chloride channel gClC-1 mRNA, partial cds	0.54	1781344	(Y10438) FK506 polyketide synthase	0.95
449	U36795	Myxococcus xanthus rfbABC O-antigen biosynthesis operon, rfbA, rfbB, and rfbC genes, complete cds.	0.54	3877232	(Z81540) predicted using Genefinder	0.74
450	AF053091	Drosophila melanogaster eyelid (eld) mRNA, complete cds	0.54	2144110	zinc finger protein RIZ - rat >gi|949996	0.14
451	V00602	Genome of the bacteriophage fd (Inoviridae).	0.54	2661620	(AL009197) hypothetical protein	0.11
452	U60800	Human semaphorin (CD100) mRNA, complete cds	0.54	125682	KERATIN, ULTRA HIGH-SULFUR MATRIX PROTEIN (UHS KERATIN) >gi|109116|pir||A36686 ultra-high-sulfur keratin - sheep >gi|1306 (X55294) ultra high-sulphur keratin protein [Ovis aries]	0.003
453	X85969	S.coelicolor secD, secF & apt genes	0.54	3874972	(Z99709) similar to Elongation factor Tu family (contains ATP/GTP binding P-loop); cDNA EST EMBL:D76223 comes from this gene; cDNA EST yk478c5.5 comes from this gene [Caenorhabditis elegans]	7e-06
454	Y08265	H.sapiens mRNA for DAN26 protein, partial	0.54	3875131	(Z70750) similar to vanadate resistance protein transmembranous domains [Caenorhabditis elegans]	5e-12

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
455	U89613	Hydromantes platycephalus cytochrome b (cytb) gene, mitochondrial gene encoding mitochondrial protein, partial cds	0.53	<NONE>	<NONE>	<NONE>
456	AF034597	Habrobracon hebetor cytochrome oxidase II gene, partial cds; and tRNA-Asp, tRNA His, and tRNA-Lys genes, complete sequence, mitochondrial genes for mitochondrial products	0.53	<NONE>	<NONE>	<NONE>
457	K02653	Yeast (S.cerevisiae) tau repetitive element and Cys-tRNA.	0.53	<NONE>	<NONE>	<NONE>
458	X53416	Human mRNA for actin-binding protein (filamin)	0.53	2134839	bullous pemphigoid antigen 2 - human	6.2
459	M55545	Drosophila subobscura alchohol dehydrogenase (Adh) gene, and alchohol dehydrogenase (Adh-dup) gene, complete cds's.	0.53	2136865	hair keratin cysteine rich protein - sheep	2.1

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
460	U19362	Methanobacterium thermoautotrophicum methylene-tetrahydromethanopterin dehydrogenase (mtd), imidazoleglycerol-phosphate dehydrogenase (hisB), and putative ferredoxin (fdxA) genes, complete cds, orf9 gene, partial cds, orfs ...	0.53	731969	HYPOTHETICAL 91.6 KD PROTEIN IN HXT8-CRT1 INTERGENIC REGION >gi|1078261|pir||S50773 probable membrane protein YJL212c - yeast (Saccharomyces cerevisiae) >gi|496950 (Z34098) ORF [Saccharomyces cerevisiae] >gi|1015596 (Z49487) ORF YJL212c	0.54
461	AB011527	Rattus norvegicus mRNA for MEGF1, complete cds	0.53	417037	GERM CELL-LESS PROTEIN fruit fly (Drosophila melanogaster) >gi|157490 (M97933) germ cell-less protein [Drosophila melanogaster]	3e-06
462	U64313	Bacillus firmus MsyB gene, 5' upstream region and partial cds	0.52	<NONE>	<NONE>	<NONE>
463	AF008590	Caenorhabditis elegans paraquat responsive protein (CePqM132) mRNA, complete cds	0.52	<NONE>	<NONE>	<NONE>
464	L10245	Mus saxicola spermidine/spermine N1-acetyltransferase (SSAT) gene, complete cds.	0.52	<NONE>	<NONE>	<NONE>
465	AF027173	Arabidopsis thaliana cellulose synthase catalytic subunit (Ath-A) mRNA, complete cds	0.52	124263	INSULIN-LIKE GROWTH FACTOR IB PRECURSOR (IGF-IB) (SOMATOMEDIN C) >gi|69361|pir||IGHU1B insulin-like growth factor IB precursor - human prepropeptide [Homo sapiens]	7.7

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
		Caenorhabditis				
466	AL021066	elegans cosmid H31B20, complete sequence [Caenorhabditis elegans]	0.52	2589162	(D88451) aldehyde oxidase [Zea mays]	6.0
467	AF038588	Porphyra linearis 18S ribosomal RNA gene, 3' partial sequence	0.52	1055055	(U39850) coded for by C. elegans cDNA yk37g1.5; coded for by C. elegans cDNA yk5c9.5; coded for by C. elegans cDNA yk1a9.5; alternatively spliced form of F52C9.8b	4.6
468	AE001125	Borrelia burgdorferi (section 11 of 70) of the complete genome	0.52	4115827	(AB021287) polyprotein [Hepatitis G virus]	2.0
469	AF006640	Drosophila melanogaster Ste20-like protein kinase mRNA, complete cds	0.52	1109830	(U41534) coded for by C. elegans cDNA CEESI42F; Similar to helicases of SNF2/RAD54 family. [Caenorhabditis elegans]	0.002
470	U90177	Aplysia californica ubiquitin carboxyl-terminal hydrolase (Ap-uch) mRNA, complete cds	0.51	<NONE>	<NONE>	<NONE>
471	Z28304	S.cerevisiae chromosome XI reading frame ORF YKR079c	0.51	<NONE>	<NONE>	<NONE>
472	Z92837	Caenorhabditis elegans cosmid R03E1, complete sequence [Caenorhabditis elegans]	0.51	123506	HYDROPHOBIC SEED PROTEIN (HPS)	7.6
473	D13803	Mouse mRNA for RecA-like protein MmRad51, complete cds	0.51	3327228	(AB014607) KIAA0707 protein [Homo sapiens]	4.5
474	X07187	Pea hsp21 mRNA	0.51	3328678	(AE001299) hypothetical protein [Chlamydia trachomatis]	4.4

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
475	S63168	CCAAT/enhancer-binding protein delta=transcription factor CRP3 homolog [human, prostate carcinoma cell line LNCaP, Genomic, 1594 nt]	0.51	1653215	(D90911) apolipoprotein N-acyltransferase [Synechocystis sp.]	1.2
476	U67078	Xenopus laevis C2-HC type zinc finger protein X-MyT1 mRNA, complete cds	0.51	3850320	(AF067520) PITSLRE protein kinase beta SV2 isoform [Homo sapiens]	0.17
477	L38933	Homo sapiens GT198 mRNA, complete ORF	0.51	3219965	HYPOTHETICAL 100.6 KD TRP-ASP REPEATS CONTAINING PROTEIN C2C6.04C IN CHROMOSOME I	0.059
478	AF001000	Lycopersicon esculentum polygalacturonase 1	0.50	<NONE>	<NONE>	<NONE>
479	Z28304	S.cerevisiae chromosome XI reading frame ORF YKR079c	0.50	<NONE>	<NONE>	<NONE>
480	X97225	Oncorhynchus keta IGF-II gene	0.50	<NONE>	<NONE>	<NONE>
481	AJ001388	Homo Sapiens, RP58 cDNA for complete mRNA	0.50	<NONE>	<NONE>	<NONE>

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
481	AJ001388	Homo Sapiens, RP58 cDNA for complete mRNA	0.50	<NONE>	<NONE>	<NONE>
482	M86626	P.occultum 23S ribosomal RNA, partial cds.	0.50	<NONE>	<NONE>	<NONE>
483	U76523	Sambucus nigra lectin precursor mRNA, complete cds	0.50	1722856	CHROMOSOME ASSEMBLY PROTEIN XCAP-E African clawed frog >gi|563814 (U13674) XCAP-E [Xenopus laevis]	3.2
484	AF031663	Mus musculus striatin mRNA, complete cds	0.50	179521	(M63730) BPAG2 [Homo sapiens]	3.2
485	U32729	Haemophilus influenzae Rd section 44 of 163 of the complete genome	0.50	3875699	(Z92829) F10A3.15 [Caenorhabditis elegans]	0.65
486	AF067198	Dictyostelium discoideum clone 9.10 Tdd-3 and RED repetitive elements, partial sequence	0.50	2494740	HYPOTHETICAL 28.3 KD PROTEIN IN GBD 5'REGION (ORF4) >gi|2120954|pir||I39562 ORF4 - Alcaligenes eutrophus >gi|695274 (L36817) ORF4	0.008
487	M23442	Human interleukin 4 (IL-4) gene, complete cds.	0.49	<NONE>	<NONE>	<NONE>
488	U16367	Caenorhabditis elegans POU homeobox protein CEH-18 (ceh-18) mRNA, complete cds.	0.47	3786409	(AF098499) contains similarity to Saccharomyces cerevisiae MAF1 protein (GB:U19492) [Caenorhabditis elegans]	8.9
489	AF001000	Lycopersicon esculentum polygalacturonase 1	0.45	<NONE>	<NONE>	<NONE>
490	Z18920	Yersinia enterocolitica wbb gene cluster	0.41	<NONE>	<NONE>	<NONE>
491	D86983	Human mRNA for KIAA0230 gene, partial cds	0.35	206712	(M64793) salivary proline-rich protein [Rattus norvegicus]	4e-05
492	AF064030	Helianthus tuberosus lectin 2 mRNA, complete cds	0.33	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
493	AF067083	Vitreoscilla sp. outer membrane protein homolog gene, complete cds; Trp repressor binding protein gene, partial cds; and unknown genes	0.33	401553	HYPOTHETICAL 24.5 KD PROTEIN IN NADB-SRMB INTERGENIC REGION	8.3
494	Y15520	Papio hamadryas anubis gene encoding fertilin alpha-II	0.29	2408049	(Z99164) hypothetical protein	3.1
495	U33475	Alestes sp. ependymin mRNA, partial cds	0.28	3913078	ARYL HYDROCARBON RECEPTOR NUCLEAR TRANSLOCATOR HOMOLOG (DARNT) (TANGO PROTEIN) transcription factor [Drosophila melanogaster]	1.4
496	D88356	Mouse DNA for 8-oxodGTPase, complete cds	0.22	<NONE>	<NONE>	<NONE>
497	U67603	Methanococcus jannaschii section 145 of 150 of the complete genome	0.22	2209261	(U51222) p40 [Streptomyces halstedii]	8.3
498	U82386	Malurus cyaneus microsatellite McyU2	0.22	992631	(U29131) Mg-chelatase subunit [Synechocystis sp.]	0.56
499	Z49625	S.cerevisiae chromosome X reading frame ORF YJR125c	0.21	<NONE>	<NONE>	<NONE>
500	U64830	Dictyostelium discoideum AX2 protein tyrosine kinase gene, complete cds.	0.21	<NONE>	<NONE>	<NONE>
501	M24543	Human prostate-specific antigen (PA) gene, complete cds.	0.21	2764859	(X97918) gene 12.1 [Bacteriophage SPP1]	6.0

SEQ ID	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
502	X87618	B.taurus mRNA for thrombospondin (partial) 2162 bp	0.21	2146000	u0002b protein - Mycobacterium tuberculosis tuberculosis] >gi|1694863|gnl|PID|e283373 (Z83018) hypothetical protein Rv2968c [Mycobacterium tuberculosis]	3.5
503	X71591	B.taurus microsatellite sequence INRA048	0.21	1354453	(U52830) orf [Homo sapiens]	2.7
504	X57808	Human germline immunoglobulin lambda light chain gene	0.21	2119158	procollagen type V alpha 2 - mouse >gi|309181	2.7
505	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.21	2497139	HYPOTHETICAL 78.8 KD PROTEIN IN ABF2-CHL12 INTERGENIC REGION >gi|1078003|pir||S52835 hypothetical protein YMR075w - yeast (Saccharomyces cerevisiae) >gi|763022 (Z48952) unknown [Saccharomyces cerevisiae]	2.0
506	U84216	Mycobacterium fortuitum plasmid pJAZ38 replication protein Rep (rep) gene, complete cds	0.21	2499087	UDP-GLUCOSE:GLYCOPROTEIN GLUCOSYLTRANSFERASE PRECURSOR (DUGT) glucosyltransferase - fruit fly (Drosophila sp.) glucosyltransferase precursor [Drosophila melanogaster]	0.003
507	U31463	Rattus norvegicus nonmuscle myosin heavy chain-A mRNA, complete cds.	0.21	3880111	(Z81130) predicted using Genefinder	0.002
508	X51508	Rabbit mRNA for aminopeptidase N (partial)	0.21	630864	LRR47 protein - fruit fly (Drosophila melanogaster) >gi|415947 (X75760) LRR47 [Drosophila melanogaster]	1e-06
509	AF086476	Homo sapiens full length insert cDNA clone ZD88F12	0.20	<NONE>	<NONE>	<NONE>
510	AF077006	Helicobacter pylori plasmid pHPM186, complete sequence	0.20	<NONE>	<NONE>	<NONE>
511	X75480	E.gunnii CAD gene.	0.20	<NONE>	<NONE>	<NONE>

SEQ ID	Nearest Neighbor (BlastN vs. Genbank) ACCESSION	DESCRIPTION	P VALUE	Nearest Neighbor (BlastX vs. Non-Redundant Proteins) ACCESSION	DESCRIPTION	P VALUE
512	X75036	T.aestivum mitochondrial nad7 gene for NADH dehydrogenase subunit 7	0.20	<NONE>	<NONE>	<NONE>
513	D90875	E.coli genomic DNA, Kohara clone #422(55.5-55.8 min.)	0.20	<NONE>	<NONE>	<NONE>
514	Z68343	Caenorhabditis elegans cosmid F59B8, complete sequence [Caenorhabditis elegans]	0.20	<NONE>	<NONE>	<NONE>
515	X62486	M.musculus V alpha 11.1 gene 5'-region	0.20	<NONE>	<NONE>	<NONE>
516	AF040651	Caenorhabditis elegans cosmid W04H10	0.20	1170683	PHOSPHORYLASE B KINASE ALPHA REGULATORY CHAIN, SKELETAL MUSCLE ISOFORM (PHOSPHORYLASE KINASE ALPHA M SUBUNIT) >gi|2135923|pir||I38111 phosphorylase kinase (EC 2.7.1.38) - human >gi|791043	7.4
517	U10470	Pseudomonas fluorescens PHA depolymerase (phaZ) gene, complete cds.	0.20	3721862	(AB016024) Pfj2 [Plasmodium falciparum]	1.9
518	D83778	Human mRNA for KIAA0194 gene, partial cds	0.20	126363	LAMININ ALPHA-1 CHAIN PRECURSOR precursor - human	0.65
519	S43579	c-scr=pp60c-src, sdr=src downstream region	0.20	4159887	(AC004908) similar to ribosomal protein L23a; similar to P29316 (PID:g132848) [Homo sapiens]	0.52
520	U07357	Mus musculus Balb/c brain-specific kinase (Bsk) mRNA, complete cds.	0.20	206712	(M64793) salivary proline-rich protein [Rattus norvegicus]	0.51

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
521	AF034460	Penicillium thomii internal transcribed spacer 1, 5.8S ribosomal RNA gene and internal transcribed spacer 2, complete sequence; and 28S ribosomal RNA gene, partial sequence	0.20	114136	AMINO-ACID ACETYLTRANSFERASE Pseudomonas aeruginosa >gi|151036 (M38358) N-acetylglutamate synthase [Pseudomonas aeruginosa]	0.39
522	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.20	2842674	POU DOMAIN CLASS 2, ASSOCIATING FACTOR 1 (B-CELL-SPECIFIC COACTIVATOR OBF-1) (OCT BINDING FACTOR 1) (BOB-1) (OCA-B) Bob1, B-cell-specific - mouse >gi|1881818|bbs|179852 mBob1=B-cell specific transcriptional coactivator line J558L, Peptide, 256 aa] >gi|1353792 (U43788) Oct binding factor 1 [Mus musculus]	0.073
523	X95971	S.lividans groEL2 gene	0.20	3925277	(AL032643) similar to Uncharacterized protein family UPF0034, Double-stranded RNA binding motif; cDNA EST yk489b3.5 comes from this gene; cDNA EST yk439g7.5 comes from this gene [Caenorhabditis elegans]	4e-19
524	L41502	Ovis aries vasopressin V1 receptor (V1R) gene, complete cds	0.19	<NONE>	<NONE>	<NONE>
525	J03885	K.pneumoniae oxalacetate decarboxylase alpha subunit gene, complete cds.	0.19	<NONE>	<NONE>	<NONE>
526	AE001451	Helicobacter pylori, strain J99 section 12 of 132 of the complete genome	0.19	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
527	D88084	Pedicularis verticillata chloroplast DNA, intergenic region between trnT(UGU) and trnL(UAA)5'exon	0.19	<NONE>	<NONE>	<NONE>
528	U67599	Methanococcus jannaschii section 141 of 150 of the complete genome	0.19	<NONE>	<NONE>	<NONE>
529	J05500	Human beta-spectrin (SPTB) mRNA, complete cds.	0.19	<NONE>	<NONE>	<NONE>
530	Y10137	M.mycoides ftsY gene homologue and gene encoding hypothetical protein	0.19	<NONE>	<NONE>	<NONE>
531	AF027174	Arabidopsis thaliana cellulose synthase catalytic subunit (Ath-B) mRNA, complete cds	0.19	<NONE>	<NONE>	<NONE>
532	D43805	Mouse thymic stromal cell mRNA for TLSF-beta, complete cds	0.19	<NONE>	<NONE>	<NONE>
533	AJ012585	Tetrahymena thermophila macronuclear gene encoding ribosomal protein L3, exons 1-2	0.19	<NONE>	<NONE>	<NONE>
534	X51475	Brassica napus 5-enolpyruvylshikimate-3-phosphate synthase gene	0.19	<NONE>	<NONE>	<NONE>
535	AF074386	Sambucus nigra hevein-like protein mRNA, complete cds	0.19	<NONE>	<NONE>	<NONE>
536	Z49625	S.cerevisiae chromosome X reading frame ORF YJR125c	0.19	<NONE>	<NONE>	<NONE>

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
537	X63741	H.sapiens pilot mRNA	0.19	<NONE>	<NONE>	<NONE>
538	Y11255	O.latipes mRNA for annexin max4	0.19	<NONE>	<NONE>	<NONE>
539	L63537	Oncorhynchus mykiss (clone Jb-10) beta-2 microglobulin (B2m) mRNA, complete cds.	0.19	<NONE>	<NONE>	<NONE>
540	X70903	N.tobacum T92 gene for auxin-binding protein	0.19	<NONE>	<NONE>	<NONE>
541	U61958	Caenorhabditis elegans cosmid C25A8	0.19	<NONE>	<NONE>	<NONE>
542	U33959	Macaca fascicularis fertilin beta mRNA, complete cds	0.19	<NONE>	<NONE>	<NONE>
543	Z49835	H.sapiens mRNA for protein disulfide isomerase	0.19	2113940	(Z95556) hypothetical protein Rv2507	9.4
544	AF035458	Spinacia oleracea heat shock 70 protein protein, complete cds	0.19	267293	PROBABLE E4 PROTEIN papillomavirus (type 1) >gi|61015 (X62844) E4 gene product [Pygmy chimpanzee papillomavirus type 1]	9.4
545	U23441	Tetrahymena thermophila B internal deletion sequence.	0.19	3877185	(Z66563) F46C3.2 [Caenorhabditis elegans]	9.3
546	U53921	Pneumocystis carinii major surface glycoprotein	0.19	3548901	(AF052502) DA26 homolog [Epiphyas postvittana nucleopolyhedrovirus]	9.3
547	L11002	Rat ankyrin binding glycoprotein-1 related mRNA sequence.	0.19	3337352	(AC004481) putative chromatin structural protein Supt5hp	9.1
548	U67560	Methanococcus jannaschii section 102 of 150 of the complete genome	0.19	3183689	(Y13585) serotonin receptor 4 [Cavia porcellus]	8.7
549	U18424	Mus musculus bacteria binding macrophage receptor MARCO mRNA, complete cds.	0.19	3659853	(AF089083) complement component C1qB like protein	7.1

	Nearest Neighbor (BlastN vs. Genbank)			Nearest Neighbor (BlastX vs. Non-Redundant Proteins)		
SEQ ID	ACCESSION	DESCRIPTION	P VALUE	ACCESSION	DESCRIPTION	P VALUE
550	X66467	C.albicans sec18 gene	0.19	1326385	(U58751) C07G1.7 gene product [Caenorhabditis elegans]	6.9
551	AF003487	Syngaster lepidus 16S ribosomal RNA gene, partial sequence	0.19	3122039	DIHYDROPYRIMIDINASE (DHPASE) dihydropyrimidinase - rat >gi|1378019|gnl|PID|d1010479	6.9
552	J05087	Rat calmodulin-sensitive plasma membrane Ca2+-transporting ATPase (PMCA3) mRNA, complete cds.	0.19	422462	hypothetical protein - fruit fly (Drosophila melanogaster) >gi|296434 (X68408) ORF [Drosophila melanogaster]	5.3
553	AF080464	Homo sapiens glutamate oxaloacetate transaminase	0.19	3024834	PROBABLE E4 PROTEIN >gi|790898 position 3286..3288 is first start codon; putative	5.3
554	U78876	Human MEK kinase 3 mRNA, complete cds	0.19	1710445	(U78083) unknown [Emericella nidulans]	5.3
555	AB009077	Vigna radiata mRNA for proton pyrophosphatase, complete cds	0.19	3256922	(AP000002) 256aa long hypothetical protein [Pyrococcus horikoshii]	5.1
556	U95098	Xenopus laevis mitotic phosphoprotein 44 mRNA, partial cds	0.19	4226159	(AF125463) contains similarity to BTB (also known as BR-C/Ttk) domains (Pfam:PF00651, Score=62.8, E=7.6e-15, N=1) [Caenorhabditis elegans]	4.1
557	AE000392	Escherichia coli K-12 MG1655 section 282 of 400 of the complete genome	0.19	3645960	(AL031583) 1-evidence=predicted by content; 1-method=genefinder;084; 1-method_score=47.46; 1-evidence_end; 2-evidence=predicted by match; 2-match_accession=SWISS-PROT:P23792; 2-match_description=DISCONNECTED PROTEIN.; 2-matc...	4.0